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INTERNATIONAL ABSTRACT OF SURGERY

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# COLLECTIVE REVIEW

## THE ORTHOPTIC TREATMENT OF STRABISMUS

### Review of the Literature from 1935 to 1939

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THE orthoptic treatment of strabismus, for the years from 1935 through 1939, has engaged the interests of American and British workers mainly, although a few references are found in the literature of other countries. There is considerable unanimity of opinion in published reports as to the general worth of orthoptics, although the extent to which it should be used in the office and in clinic practice has not yet been agreed upon by investigators.

Orthoptics, of course, is not a new measure in the treatment of squint (10). Non-surgical measures were attempted as early as 1870. Javal and Remy were the pioneers, followed by Claude Worth. The stereoscope was the instrument used almost entirely by Javal, and, indeed, was all that was available until Worth developed the amblyoscope. Most authorities are agreed that the stereoscope has certain limitations for effective therapy. The limitations of the original amblyoscope were many, also; therefore, not until the more modern modifications of the stereoscope and amblyoscope became available (since 1914) did orthoptics begin to receive more general acceptance by ophthalmologists.

There is considerable agreement as to the purpose of orthoptics. Mayou (33) and Hicks (27) say that its purpose is to develop binocular vision. Davis (13) says that "orthoptics is a valuable and essential aid in the cure of squint." Peter (38) gives as the objects, "the restoration of vision; the correction of suppression; parallelism in visual axes; and the development of fusion." On the other hand, Daily (12) considers orthoptics as an aid to surgery and uses it as such.

#### SELECTION OF PATIENTS

If binocular vision is to be obtained, Hicks (27) claims that the following conditions must be fulfilled: (1) there must be good monocular fixation and projection in each eye; (2) the visual acuity in the eyes must be approximately equal; (3) an image of approximately the same size and shape must be received from each retina, and corresponding retinal points must be able to function in association with each other; (4) there must be a large overlapping field of vision and only partial decussation of the optic tracts (in man as opposed to lower animals); (5) the neuromuscular mechanism of each eye must function normally alone and in association with the fellow eye; and (6) the higher cerebral centers must be fully capable of fusing the two monocular sensations.

The patients for orthoptic training should be selected, for there are certain contraindications to this type of training. Even so, Wurdemann (52) agrees with Cantonnet and Filliozat that orthoptics can cure 70 per cent of patients with squint, and Emerson (17) thinks that 75 per cent of the patients with squint are suitable for orthoptics. Bressler (10) lists the following factors to be considered in selecting patients suitable for orthoptic training:

1. Age; the patient should be at least seven or eight years old.

2. Degree of deviation; the most favorable cases have less than 25 degrees; in those with more than 35 degrees cure should not be attempted by orthoptics only.

3. Visual acuity; the deviating eye must have at least 20/65 vision, or in rare cases vision may be 20/100.

4. Excursion of eyes; deviations due to paralyses or cicatricial contraction of the ocular muscles make the patient unsuitable for orthoptic treatment.

5. Degree of suppression; if the suppression is very difficult to overcome, the prognosis will be poor.

In addition, the patient must be of average intelligence and must be willing to attend treatment sessions regularly. Gifford (19) and Guibor (23) consider 20/80 as the minimal visual acuity necessary in the squinting eye; Penman (37) considers it to be 6/18, and Sverdlick (46) 3/10. The last also lists the type of cases which he considers unsuitable for training. These include cases with loss of central fixation, with paresis, with deviations of more than 30 degrees, cases of anisometropia of more than 5 D, and of myopia of more than 10 D. We believe that many patients with the last two conditions may be helped by orthoptics and should not be excluded on this basis. Abraham (1) claims that fusion therapy should not be attempted with less than 20/70 vision in the poor eye because fusion developed in the presence of amblyopia is abnormal and may not be maintained.

### STEPS IN ORTHOPTIC TREATMENT

Orthoptic treatment may be divided into the broad classifications of refraction, the treatment of amblyopia, the treatment of false projection and suppression, and fusion training. It is assumed that before it is started a careful history has been taken and ocular examination, including measurement of the deviation, has been carefully done.

*Refraction.* Travers (49) summarizes the accepted principles of refraction of squint. Convergent squint with hyperopia should be fully corrected. Astigmatism and myopia should be fully corrected also, but divergent squint with hyperopia should be undercorrected. Refraction should be done under atropine. Gifford (19) advises following Guibor's method of treatment of the accommodative types of convergent squint by full correction and the use of a paster bifocal for near work. The patient's eyes are kept under atropine, and fusion training is given at the same time.

*The treatment of amblyopia.* The principle of treatment of amblyopia is occlusion of the fixing eye. This may be partial, as with atropinization or frosted glass, or complete with an opaque occluder. The younger the patient is when treatment is instituted the better the chances are for success. Mayou (33) considers the optimum age to be five or six years. Goulden (20) and Worth say results of treatment are poor if the patient is more than six years old; Pugh and Jackson, more than twelve; and Sattler, more than fourteen (cited in 12). Peter (38) says that amblyopia ex anopsia can be cured in most patients up to the age of seven and that cures diminish up to the age of twenty. Daily (12) believes that it is not so much the age that causes the poor results as the difficulty of maintaining occlusion in older children. He uses continuous total occlusion until the vision is 20/40 and then partial occlusion. Lyle and Jackson (31), Pugh (41), and Travers (49) advise complete continuous occlusion for higher degrees of amblyopia (6/18 or less). Gifford (19) was unsuccessful in obtaining complete occlusion, finding it impossible when vision was less than 20/200. He advises occlusion for from one to two hours a day and atropinization of the good eye. Daily (12) and Hitz (28) did not find atropinization of the good eye of value in improving vision unless the vision in the poor eye was at least 20/50. A lone dissenter was Wurdemann (52) who found constant occlusion "of little avail." He advised "exercising" the amblyopic eye "with test letters."

The results of treatment of amblyopia ex anopsia are encouraging. Davis (13) found that 37 per cent of 46 clinic amblyopic cases and 81 per cent of 15 private cases improved (as was shown by the ability of the patient to read 2 or more lines more than he had before treatment was instituted). Penman (37) reports that of 42 patients in whom occlusion was done 35 showed improvement to a visual acuity of 6/9 or better, and of 143 patients in whom occlusion was done for three months at the Royal Westminster Ophthalmic Hospital, only 14 showed no improvement. Berens (4) studied 85 private and clinic patients. Fifty-seven patients were between the ages of three and eight; 18 between the ages of nine and twelve and 10 between the ages of thirteen and twenty-one. Vision was improved in 36, or 63 per cent, of the first group, in 12, or 67 per cent, of the second group, and in 5, or 50 per cent, of the last group.

*False projection.* False projection has been defined by Bielschowsky (7) as "a functional adaptation of the sensory apparatus to the abnormal position of the eyes relative to a fixed object";

by Pugh (41) as "a mental reorientation of the displaced image"; and Worth says that " . . . the mind sometimes learns to make full allowance for the faulty position of this (the deviating) eye. So that the eccentric image, formed in the deviating eye, is mentally projected to the same spot as the true macular image, formed in the normally directed eye, and is blended with it." Verhoeff (50) prefers the term anomalous projection and defines it as "a type of binocular projection in which there are no corresponding visual axes, or as a type of binocular projection without retinal correspondence."

There is a high incidence of false projection. Smith (45) estimates that over 50 per cent of the patients with convergent squint have it (94 of 177 patients); Travers (49) found an incidence of 40 per cent in 154 patients; Bryant (11) found it in 50 per cent of 200; and Mayou (33) found it in 50 per cent of 300.

The diagnosis is most readily made on one of the easily adjustable major amblyoscopes, the synoptophore, or a similar instrument (45). The true angle of the patient's deviation is determined by screening, either with prisms or on the instrument. Two dissimilar test objects are then placed before the patient's eye at this angle. If projection is normal the two images will be superimposed. If false projection is present, the two images will be separated. The instrument is then adjusted so that the images become superimposed or approach each other as near as possible without crossing over and the difference in prism diopters between the objective and the subjective angles is noted. "If this discrepancy is greater then 5 prism diopters, the diagnosis of false projection is justified" (45).

The actual treatment (as practiced by all workers) for the re-establishment of normal projection is the simultaneous stimulation of both maculæ. This is best carried out on a synoptophore, or like instrument, and consists of presenting images to both maculæ with the arms of the instrument set at the true deviation. These are manipulated in any manner which will attract and hold foveal fixation.

Pugh (42) makes this general statement as to the possible effects of false projection: "If a patient's eyes are straightened by operation while he is still using false projection, he may after operation do one of three things; (a) He may, finding the visual axes parallel, develop a true projection and fuse with his eyes straight; (b) He may pass through a transitional stage when he learns to readjust his projection so that he eventually adapts himself to the new position of the eyes. During this stage there is a false diplopia . . . ; (c) He may show no signs of modifying his false projection, but retain it. Such a patient suffers from a troublesome false diplopia and in his efforts to overcome this symptom he reverts more or less to his original deviation."

Smith (45) found that many of the failures in the operative cases of squint at the Wilmer Ophthalmological Institute might be attributed to lack of restoration of normal projection before operation. In 30 cases operated on before false projection was corrected, the eyes of only 4 patients remained straight; while in 19 of those operated on after false projection was corrected the eyes of 17 remained straight. Daily (12), also, believes that false projection accounts for most of the poor surgical results. Berens (4) states, "It has been my experience that, unless true projection takes place before operation, the same degree of deviation which existed prior to intervention may recur. . . . Nevertheless, in certain cases in which normal retinal correspondence could not be developed pre-operatively, operation followed by continuous orthoptic training was apparently of benefit in producing normal retinal correspondence. Of 126 clinic patients, 33 (25%) had false projection before orthoptic training while only 13 (10%) had false projection following." In the orthoptic department of the New York Eye and Ear Infirmary at the present time, treatment is successful in restoring true projection in about 85 per cent of the cases of false projection. On the other hand, Travers (49) met with very discouraging results in the treatment of false projection and believes that operation is the only method which has given any satisfactory results. Anderson (2) was successful in restoring true projection in only 33 per cent of 33 patients.

The length of time that patients are treated for the development of true projection and the age at which they are treated is not always stated. Also the frequency with which patients receive treatment, and the individual giving the treatment, are factors which have been stressed by Berens as possibly accounting for differences in the published results of treatment. His office patients (Personal Communication, 53) received daily treatment at home under the supervision of trained technicians both before and after operation, and the training periods sometimes lasted over a period of seven or eight years. Whether the patients were really trained, and the time when it is possible to train patients with abnormal retinal correspondence are all-important points. He believes the major amblyoscopes are the most useful instruments for this type of work.

*The treatment of suppression.* After amblyopia and false projection have been treated, suppression must be considered. Suppression may be present without having been preceded by either of the former conditions. It may be complete or partial and may be a matter of intensity as well as area (31), that is, the patient may fuse the gross details of the two slides (49), but may suppress certain finer details. For example, in slides of a horse with spots, he might see the outline of the horse readily enough but suppress some of the spots.

Diagnosis may be made by means of slides in the synoptophore; with the arms of the instrument set at the patient's angle of squint only one of the slides will be seen and not the other. Or the Worth 4-dot test (31) may be used. In this test four panes of glass are arranged in a diamond formation illuminated from behind. The two lateral ones are green, the upper one red, and the lower white. The patient wears a red glass in front of one and a green glass in front of the other eye. The test is made with the patient at 5 meters. If he has single binocular vision, he will see four lights, two green, one red, and one a mixture of greenish red. If he has binocular vision but his visual axes are not parallel he will see five lights, three green and two red. If he is suppressing with one eye he will see either three green or two red lights according to which eye is being suppressed.

Berens (5) has recently modified this test, particularly for use with small children. Three characters, an elephant, a sail boat, and a child with outstretched arms, are used instead of the round dots.

Treatment of suppression, as in that of false projection, is directed toward the simultaneous stimulation of both maculæ. This is most conveniently done with one of the major amblyoscopes (41). The instrument is set at the true angle of the squint and the patient directed to look with both eyes at dissimilar pictures, such as an auto and a garage. The light may be dimmed before the fixing eye and increased before the suppressing eye. The slide before the suppressing eye is moved and the arm of the instrument moved backward and forward so that the image is constantly crossing the macula. Occlusion of the suppressing eye may be carried on along with other treatment. Drawing with the cheiroscope (31) is also of value in overcoming the suppression.

*The development of fusion.* Worth's gradation of binocular vision is generally used. The first stage is simultaneous macular perception with normal projection. As Travers (49) points out, it is not enough to say that the first stage of binocular vision is "simultaneous macular perception" because many cases of false projection have this and yet do not have the first stage of binocular vision. The second stage is fusion of similar images, the blending of similar images by the two eyes into one. The third is stereoscopic vision, the blending of slightly dissimilar images with depth perception.

The instrument most favored for fusion training is one of the major amblyoscopes, the synoptophore or orthoptoscope (41, 49, 31, 33). The stereoscope is advocated as a training instrument by Guibor (25), Gifford (19), and Russell (43), but Bressler (10), and Peter, Wilkinson, and Wells (39) believe that the stereoscope has only a limited place in orthoptics. Other instruments which may be of aid are the cheiroscope, the myoscope, the diploscope, and several varieties of stenoscopes (31).

There is general agreement that the actual orthoptic training is best carried out by trained technicians under medical supervision (10), and that the treatments should be individual and not group treatments. Three treatment periods of thirty minutes each are advised (10, 31), although daily treatments are to be preferred (22), particularly postoperatively. Home treatment is generally unsatisfactory and is limited to patients who have true projection, as an adjunct to office training to break down suppression and to develop fusion after it has begun.

The technique as advocated by Lyle and Jackson (31) is as follows:

The slides used in the amblyoscope for the development of first-grade fusion have been described; they are of dissimilar objects, such as a lion and a cage. Those used for second-grade training contain similar objects with one or two dissimilar details, e.g., a cat with a tail missing in one slide and ears missing in the other. When a single cat with ears and tail is seen one knows the patient is fusing the two. However, Feldman (18) believes that second-grade fusion is best developed by the use of color slides, e.g., yellow and blue cards. Gifford (19) found that simple figures showing perspective, and not flat pictures, were the easiest to fuse, such as found in the Wells "E" series, and Guibor's cards. Once the second stage has been reached "amplitude" is worked for; i.e., the patient is urged to keep the two images together while the arms of the instrument are moved to introduce prism base in or out. It is important also in accommodative squints to train the patient to dissociate accommodation and convergence. This is done by having him go

without his correction during training periods and to practice "seeing misty" as he would with relaxed accommodation. Third-grade fusion or stereopsis is developed by having the patient study stereograms in the amblyoscope or stereoscope and having him try to see differences in depth.

### ORTHOPTICS AND SURGERY

While it is not within the scope of this review to consider the surgical correction of squint, the relationship of orthoptics to surgery should be mentioned. Indeed, surgery may even be considered a part of the orthoptic treatment. Certainly the treatment of squint would be inadequate if one were confined to the use of either measure. Mayou (34) says that squints of more than 10 or 15 degrees, or postoperative deviations require surgery. Post (40) advises surgery before orthoptic training if the deviation is more than 15 degrees. He says nothing of amblyopic training. Lyle and Jackson (31) list among indications for operation: abnormal retinal correspondence (false projection) which is uncorrected by 24 orthoptic treatments, intractable amblyopia (cosmetic results only) and no fusion sense. Berens (6) thinks surgery is advisable if the deviation is too much for orthoptic and optic correction, if symptoms are only partially relieved by lenses and prisms, or if the underlying causes have been removed and the condition remains stationary.

### RESULTS OF ORTHOPTIC TREATMENT

The lack of uniformity in reporting cases which have received orthoptic training makes comparisons of the results of the various workers difficult. Obviously, all reports of the past five years cannot be tabulated in this review so an attempt has been made to list the larger series and those which contain records of the state of fusion.

Hicks and Hosford (27) found that among 24 cases of esotropia treated surgically but without orthoptics, fusion developed spontaneously after operation in 16, or 66 per cent. Among 36 cases receiving orthoptic training only, fusion was developed in 25, or 69 per cent.

Anderson (2) reports the following:

24 cases of esotropia averaging 14 degrees with true projection—17 (71 per cent) cured after orthoptic treatment only.

10 cases of esotropia averaging 22 degrees with true projection—5 (50 per cent) cured after orthoptic and surgical treatment.

4 cases of esotropia averaging 22 degrees with true projection—2 (50 per cent) cured after surgical treatment only.

Cure-phoria less than 5 degrees and third-grade fusion.

Berens (4) reported the results in the treatment of 223 cases of squint. Forty-nine patients received surgical treatment only. After operation 46 still had heterotropia and 3 had heterophoria and second-grade fusion. Eighty-five patients, 70 with esotropia and 15 with exotropia, received orthoptic training following surgery. Before treatment some degree of fusion was present in only 21 (24 per cent). Following surgery and postoperative orthoptic training some degree of fusion was present in 52 (61 per cent). Heterotropia persisted in 47 (55 per cent). Eighty-nine patients, 74 with esotropia and 15 with exotropia, received orthoptic training before and after surgery. Prior to treatment some degree of fusion was present in 38 (43 per cent). Following preoperative and postoperative orthoptic training some degree of fusion was present in 65 (73 per cent). Heterotropia persisted in 37 (42 per cent).

Vorisch (51) treated 245 patients with esotropia who were less than thirteen years of age by means of atropine, occlusion, and correction of the refractive error. One hundred and eighty-three (75 per cent) were monocular and 62 (25 per cent) were alternators. Of the 245, 109 (44 per cent) were cured, 68 (28 per cent) were benefited, 37 (15 per cent) were not benefited, and 31 (13 per cent) presented a worse condition after the treatment.

Mayou (34) reports 93 cases of divergent strabismus among 800 consecutive cases of squint and considers squints of less than 10 or 15 degrees or periodic squints as curable by orthoptics.

Bressler in a study of 2 series of cases found the results to be as shown in the table appearing on Page 6.

Guibor (23) studied two groups of squint cases. The first group consisted of 148 patients who were treated by correction of the refractive errors, atropinization of one or both eyes, and occlusion of the fixing eye, but they received no fusion training. The second group consisted of 65 patients who received the same treatment plus fusion training. In Group 1 recovery occurred in 70 per cent of those with the accommodative type of esotropia and in 74 per cent of those with the accommodative amblyopic type; but in only 9 per cent of those with squint associated with fusion defects and 15 per cent of those with squint associated with amblyopia. There were no recoveries in the cases of squint associated with muscular defects and muscular defects with amblyopia. In Group 2, 83 per cent of the patients with accommodative squint recovered (70 per

TABLE I.—RESULTS IN CASES OF SQUINT

| | Pre-operative | | | | Postoperative | | | |
|---|---|---|---|---|---|---|---|---|
| | Number of cases | | Percentage | | Number of cases | | Percentage | |
| | Series 1 | Series 2 | Series 1 | Series 2 | Series 1 | Series 2 | Series 1 | Series 2 |
| Group 1 (Operative treatment) Series 1—64 cases (9) Series 2—150 cases (10a) | | | | | | | | |
| Deviation 15–50° Straight | 0 | 150 | 0 | 100 | 22 | 48 | 33 | 32 |
| Fusion None | 0 | 150 | 0 | 100 | 58 | 138 | 85 | 92 |
| Fusion | | | | | 6 | 12 | 15 | 8 |
| Group 2 (Surgery and orthoptics) Series 1—59 cases Series 2—32 cases | | | | | | | | |
| Deviation Straight | *5 | *2 | 8 | 6 | 16 | 15 | 27 | 47 |
| Not straight | 54 | 30 | 0 | 0 | 43 | 17 | 73 | 53 |
| Fusion None | 50 | 29 | 88 | 91 | 38 | 8 | 64 | 25 |
| Fusion | 9 | 3 | 12 | 9 | 21 | 24 | 36 | 75 |
| Group 3 (Pre-operative and postoperative orthoptics) Series 1—40 cases Series 2—36 cases | | | | | | | | |
| Deviation Straight | 0 | 0 | 0 | 0 | 17 | 20 | 42 | 56 |
| 15–45° | 40 | 36 | 100 | 100 | 23 | 16 | 58 | 44 |
| Fusion None | 24 | 29 | 60 | 81 | 11 | 7 | 27 | 9 |
| Fusion | 16 | 7 | 40 | 19 | 29 | 20 | 73 | 81 |

Series 1(9)—kind of squint not stated.
Series 2—171 cases of esotropia and 27 cases of exotropia.

*Apparently refers to deviation after surgery and before orthoptics.

cent, Group 1), 40 per cent of those with the amblyopic type of squint (15 per cent, Group 1), 15 per cent of those with a muscular defect (0, Group 1), and 22 per cent of those with muscular defects and the amblyoscopic type of squint (0, Group 1).

A National Orthoptic Board has been appointed at the suggestion of the American Committee on Optics and Visual Physiology and orthoptic-training technicians are now certified by this Board. This has been one of the factors which is leading to greater acceptance of orthoptic training. Since technicians and equipment have been available in certain of the large hospitals, for example, the New York Eye and Ear Infirmary, Johns Hopkins Hospital, Wills Hospital, and Illinois Charitable Eye and Ear Hospital, men are having a better opportunity of becoming acquainted with the use of certain instruments and the methods of managing certain types of heterophoria and heterotropia.

There has been an awakening of interest in orthoptics in the past six years but there is a need for careful reports of the results obtained. This is true particularly in reference to false projection, concerning which relatively little has been reported.

I wish to express my appreciation to Doctor Conrad Berens for his helpful suggestions in preparing this review, and to the Ophthalmological Foundation, Inc. for secretarial work.

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# ABSTRACTS OF CURRENT LITERATURE

## SURGERY OF THE HEAD AND NECK

### EYE

**Gifford, S. R.: The Treatment of Secondary Glaucoma.** *Arch. Ophth.*, 1940, 23: 301.

The author points out that the treatment of secondary glaucoma, even more than that of primary glaucoma, is a matter of individualization. Judgment and experience are required as in few other conditions, together with versatility and the courage to follow out clinical indications without loss of time.

Most important is early recognition of the condition, for which nothing is more essential than use of the tonometer in every case in which the possibility of glaucoma exists.

Miotics are useful, and it would seem that mecholyl may prove a valuable recent addition to this category.

Epinephrine and its derivatives, though dangerous during active iridocyclitis, are often of value in glaucoma following cataract extraction or discission.

The intravenous injection of hypertonic solutions is exceedingly useful; it may be the means of aborting an acute attack and will usually allow operation to be performed under relatively favorable conditions. It will obviate resort to paracentesis in many cases.

Operative intervention is often necessary and should be promptly employed when tension cannot be controlled by other means. The operations which proved of greatest value in this series were iridectomy for glaucoma following uveitis, and cyclodialysis for glaucoma following cataract extraction or discission.

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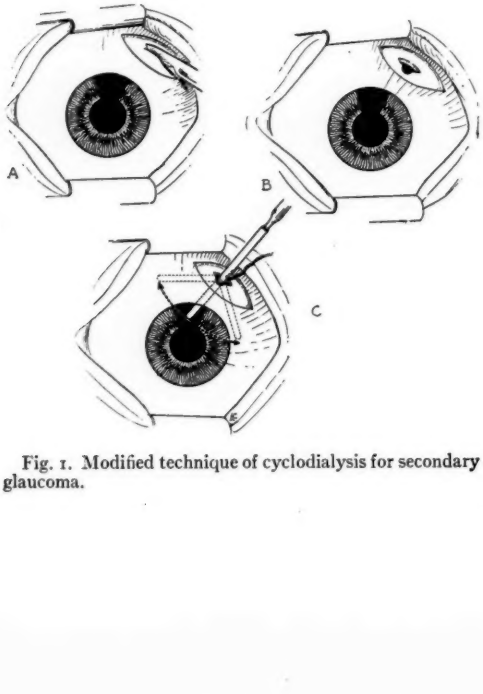



Fig. 1. Modified technique of cyclodialysis for secondary glaucoma.

**Troncoso, M. U.: Cyclodialysis with Insertion of a Metal Implant in the Treatment of Glaucoma: A Preliminary Report.** *Arch. Ophth.*, 1940, 23: 270.

Troncoso makes a real contribution to ophthalmology in this well written and well illustrated article, and backs it up with clinical and experimental research. He concludes thus:

"To improve the results of cyclodialysis in the treatment of glaucoma, I have implanted a strip of magnesium in the wound between the ciliary body and the sclera. Magnesium is absorbed by the tissues, giving off bubbles of free hydrogen, in about twenty days. The presence of the metal and the bubbles of gas prevent the reattachment of the ciliary body to

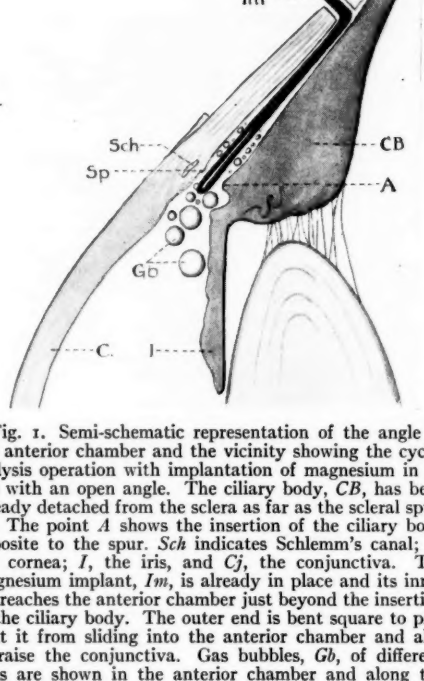



Fig. 1. Semi-schematic representation of the angle of the anterior chamber and the vicinity showing the cyclodialysis operation with implantation of magnesium in an eye with an open angle. The ciliary body, *CB*, has been already detached from the sclera as far as the scleral spur, *Sp*. The point *A* shows the insertion of the ciliary body opposite to the spur. *Sch* indicates Schlemm's canal; *C*, the cornea; *I*, the iris, and *Cj*, the conjunctiva. The magnesium implant, *Im*, is already in place and its inner tip reaches the anterior chamber just beyond the insertion of the ciliary body. The outer end is bent square to prevent it from sliding into the anterior chamber and also to raise the conjunctiva. Gas bubbles, *Gb*, of different sizes are shown in the anterior chamber and along the tunnel made by cyclodialysis.

the sclera, thus affording a new way for the outflow of the aqueous to the perichoroidal space. Experiments with animals and microscopic sections have shown that a lacunar scar is formed between the anterior chamber and the suprachoroidal space, ending in a thin scleral cicatrix. No complete channel was ever found.

"Implantation of magnesium after cyclodialysis was made in 12 human eyes with subacute, chronic congestive, simple or congenital glaucoma. There was at first a mild reaction to the foreign body, with numerous bubbles of gas appearing in the anterior chamber and under the conjunctiva. The reaction subsided in about one week, and the metal was entirely reabsorbed at the end of twenty days. Clinical results have been good in the majority of cases; in others, there was improvement with diminution of hypertension, and in 1 case no improvement occurred. The method is harmless and can be repeated several times in the same eye."

LESLIE L. MCCOY, M.D.

**Smithers, D. W.: The X-Ray Treatment of Malignant Tumors in the Region of the Eyes.** *Brit. J. Ophth.*, 1940, 24: 105.

The effect of x-rays on the eyes and the radiation methods of treatment of malignant growths in the vicinity of the eyes are discussed briefly. Previous methods of eye protection are referred to and new lead-covered contact "perspex" shells for protection of the eyes in short-distance low-voltage x-ray treatment are described. The advantages of this form of x-ray therapy and the results obtained in the treatment of tumors of the lids and canthi during the last four years at the Royal Cancer Hospital are discussed.

There is no part of the body in which greater care and accuracy are necessary in the radiation treatment of malignant tumors than the region surrounding the eyes.

The effects of radium and x-rays on the eye are essentially the same and there is an absolute relationship between the dose of radiation given and the pathological changes produced. The eyelids are slightly more radiosensitive than the surrounding skin of the face, and the conjunctiva slightly more radiosensitive than the eyelids. The cornea is distinctly less sensitive than the lids and conjunctiva, and the iris is less sensitive still. The retina and optic nerve are remarkably insensitive to irradiation. The lens, in adults, is not very susceptible to the effects of irradiation, but the late development of cataract is a serious complication that must be guarded against. There is little doubt, however, that cataract does occur as the result of irradiation, and that a five-year latent period is not uncommon.

In x-ray treatment, therefore, the immediate danger to the eye is severe conjunctivitis followed by corneal ulceration, and the late danger is the development of cataract. Treatment of tumors of the inner canthus may damage the lacrimal duct and result in troublesome epiphora.

Tumors which invade the eyeball or encroach upon the walls of the orbit are a problem apart, for their situation renders damage to the eye as a result of treatment an unavoidable risk and a secondary consideration. Tumors of the eyelids or neighboring skin are in a different category and any injury to the eye in the treatment of such tumors should now be regarded as due to a serious error in technique.

Lead is the most effective shield, for the protection that it affords increases with the density and atomic number of the element. LESLIE L. MCCOY, M.D.

**DeRötth, A.: Plastic Repair of Conjunctival Defects with Fetal Membranes.** *Arch. Ophth.*, 1940, 23: 522.

Conjunctiva has to be replaced when a large enough area is destroyed so as to cause a high degree of symblepharon or entropion, or when the socket is too small to carry a prosthesis. Most common causes of its destruction are chemical and thermic burns and trachoma.

The ideal material for replacing conjunctiva is conjunctiva itself, but only a small piece can be taken from the same patient's other eye. Other tissues that have been tried are skin, mucous membrane of the mouth, vaginal mucous membrane, vernix caseosa, and grafts from the prepuce or labia minora, but none have proved entirely satisfactory.

An ideal material for this purpose should be a thin, smooth, transparent human tissue like the conjunctiva; it should be sterile and obtainable in a sufficiently large amount.

Fetal membranes seem to have all these requirements; in addition, they are elastic and carry but few vessels, and the patient does not have to undergo another operation. The author obtained such membranes by cesarean section. The membranes were kept in tepid Locke solution from one to fifteen hours. He used this material in 6 cases of symblepharon (8 operations) and in 2 cases in which the socket had to be enlarged.

*Technique of the operation.* The conjunctiva is undermined from the limbus to the margin of the lid. The undermined conjunctiva is fixed to the lid with two or three mattress sutures to build the palpebral conjunctiva. The graft is fixed to the tendon of one or more rectus muscles, which gives a fixed point on a firm base and avoids shrinkage. The graft covers the fornix, and its edge will unite with that of the conjunctiva lining the lid. The graft is not allowed to make folds but just covers the sclera and fornix smoothly.

When fetal membranes are used the chorion surface is placed on the wound following removal of tense fibers of connective tissue, if any are present. The amnion forms the free surface. In all cases a binocular dressing was applied for three days when the bandage was first changed.

The method deserves further study for the following reasons:

1. The embryonal tissue used has the property of being transformed to conjunctiva. The epithelium

of the membranes excised two and four months after transplantation showed the same histological structure as the epithelium of the bulbar conjunctiva.

2. In the successful case the course of the new vessels in the graft was like that of a normal conjunctiva. In no other form of graft may this be observed.

3. The fetal membranes covering the cornea resulted in a shiny transparent tissue. Whether it was the graft itself or whether the graft was replaced by normal corneal epithelium, the author does not know.

At present the author thinks the use of fetal membranes should be confined in conjunctival plastic operations to cases of symblepharon when for any reason mucous membrane of the mouth is not obtainable; i.e., when there is disease of the mouth, when the patient refuses operation in the mouth, and, further, when the symblepharon includes the cornea as well, for mucous membrane of the mouth gives a poor cosmetic effect when covering the cornea.

LESLIE L. MCCOY, M.D.

**Davidson, M.: Lens Lesions in Contusions. A Medicolegal Study.** *Am. J. Ophth.*, 1940, 23: 252.

The author says, "This study deals only with the permanent lesions of the lens due to contusion."

Lens lesions from contusions give rise to frequent controversies in the administration of workmen's compensation. A survey of the problem as it presents itself in actual practice is here attempted in the form of a brief review of the literature, and of an analysis of the material dealt with in the past one and one-half years at the Bureau of Workmen's Compensation of the New York State Department of Labor.

While lens opacity and cataract are generally used as synonyms for statistical and medicolegal purposes, and particularly for the peace of mind of a patient or a claimant for compensation, the use of the term "cataract" to describe all kinds of lens opacities, regardless of their effect on visual acuity or fundus visibility or probable evolution, is confusing and highly undesirable. The writer uses the term "cataract" in this paper to describe a lens opacity only when it is so complete as not to permit an examination of the fundus.

He comes to the following conclusions:

1. The use of the term "cataract" to describe all kinds of lens opacities, regardless of their extent and effect on visual acuity, is confusing and gives rise to misunderstandings. It should be restricted to designate complete lens opacifications.

2. Our pre-slit-lamp knowledge of the lens was meager and imprecise, and the textbooks and literature of that period reveal a too considerable confusion and uncertainty in dealing with the medicolegal aspects of lens opacities and cataracts due to contusions to be invoked with propriety in medicolegal controversies.

3. The slit-lamp has taught us to recognize the specific ages of lens zones, the specific morphology of the results of mechanical injury, the fact of "remotio cataractæ traumaticæ," and has furnished us with a biomicroscopic technique of equal status with the histologist's technique. It has dispelled some previous misconceptions as to the rôle of ruptures of the posterior capsule from contusions and established their rarity; of macroscopic ruptures of the anterior capsule, found also to be rare; and of ruptures of the equatorial capsule, similarly non-demonstrable; and has served to call our attention to the biochemical rôle in the production of lens opacification, along with the mechanical factors in contusions. It has also enabled us to verify the activation of presenile and pathological processes in a lens resulting from contusion.

4. An analysis of the examination of 57 eyes with contusion lens opacities of a wide variety of ages establishes a morphological specificity of juvenile and adult contusion lesions up to the age of forty-five years, on the basis of subcapsular beginning, the tendency toward equatorial and posterior lens involvement, and regional segmentlike localization. It shows that after the age of forty-five years senile pathological changes intervene to make less discernible the specific morphology of contusion lens opacity. It is not possible to designate the age of a lens opacity with any accuracy from its depth alone because of the widely varying rate of recession into depth that has been observed. The density of an opacity resulting from compression in course of time is a more important clue than depth, but it is difficult to measure accurately.

5. The prognosis of contusion lens opacities occurring before the age of thirty is good. After that age, it should be guarded and the lesion not declared stationary until a period of observation of three years has passed, in order to take care of statutes of limitation in the administration of workmen's compensation and protect the claimant against future deteriorations.

It would be well for physicians who are confronted with medicolegal cases to study carefully this very detailed, well illustrated, and scientific treatise.

LESLIE L. MCCOY, M.D.

## EAR

**Selfridge, G.: Chronic Progressive Deafness with Special Reference to Estrogenic Substances: A Further Contribution.** *Ann. Otol., Rhinol. & Laryngol.*, 1940, 49: 52.

Selfridge believes that estrogenic substances probably play an important rôle in conduction deafness. Estrogen relieves completely in many cases the tinnitus, menstrual irregularities, and other symptoms occurring during menstruation. Unfortunately, these symptoms recur in many instances when estrogen is discontinued. There is definite evidence that thyroid as well as pituitary and adrenal-cortex is of importance in treatment. Thiamin chloride and nicotinic acid have been found to be helpful, while other factors of the $B_2$ complex, together with other vitamins, appear to be of use.

Neither nerve deafness nor conduction deafness is caused by any single factor, but it appears to be linked with the various factors related to growth, i.e., endocrine glands, vitamins, mineral salts (the electrolytes), and amino-acids. The slowly accumulating evidence points to nutritional deficiencies, and the beginnings probably occur during the period of gestation and are due chiefly to dietary errors and endocrine disturbances of the pregnant mother. The prevention of deafness, therefore, depends on the mother's getting an optimum diet containing all the essential foods during the gestation period, and such dietary habits must be carried on during babyhood, childhood, and adolescence.

Finally, the author asserts that further work is necessary concerning the various factors referred to in this and other papers already published, and especially the nutritional, endocrine, and allergic factors that may prove to be related to the enlargement of tonsils and adenoids.

NOAH D. FABRICANT, M.D.

**Harris, H. E., and Moore, P. M., Jr.: The Use of Nicotinic Acid and Thiamin Chloride in the Treatment of Ménière's Syndrome.** *Med. Clin. North Am.*, 1940, 24: 533.

The authors found a history of dietary deficiency in their cases of Ménière's syndrome. Neither thiamin chloride nor nicotinic acid alone benefited their patients but combination of the two was beneficial. They give 10 mgm. of thiamin chloride twice a day, and 50 mgm. of nicotinic acid five times a day. Post-nicotinic-acid flushing is not a contraindication. In addition, from ½ to ¾ pound of rare red ground meat, ½ pound of liver three times a week, wheat germ, raw vegetables, and raw fruit were included in the diet. Of 20 patients so treated, 17 are free of vertigo and the remainder are benefited; their hearing also has improved and the tinnitus has decreased. The recovery came gradually over a period of several weeks. PAUL STARR, M.D.

**Fischer, J.: Changes in the Internal Ear Due to Increased Endocranial Pressure: The Histological Basis of Congestive Inner Ear.** *Arch. Otolaryngol.*, 1940, 31: 391.

The question of whether changes in the inner ear, similar to choked disc in the eye, occur as a result of increased endocranial pressure has not yet been definitely answered. Likewise, the question of endocranial pressure itself is still in dispute. Differentiating between clinical symptoms and pathological anatomy due to chronic endocranial pressure, the author reports microscopic studies of the petrous temporal bone on 5 patients who died from brain tumor. Examination of these sections led to the conclusion that numerous changes in the inner ear are caused by chronic brain pressure. These can be classified into the following main groups:

1. Transudation, exudation, and lymphatic congestion within the membranous inner ear and the nerve ganglion apparatus.

2. Hyperemia (especially venous), hemorrhages, and alterations of the walls of the blood vessels within the inner ear and the petrous bone.

3. Formative changes within the membranous inner ear, in the ductus cochlearis, the ductus endolymphaticus, the ductus perilymphaticus, and the ductus reuniens.

4. Formations of hernias of the brain and pacchionian granulations.

5. Secondary (later) changes: pigmentations, attachments, and adhesions in the membranous inner ear, and ascending atrophy of the nerve ganglion apparatus.

6. Pressure atrophy of the bone due to osteoclasts and Volkmann's perforating canals, caused by herniations of the brain and pacchionian granulations.

Elaboration and a detailed discussion of these groups are then given, with a dissertation on the analogy between aural changes and choked disc as interpreted by the author. JOHN F. DELPH, M.D.

**McKenzie, W.: The Results of the Conservative Radical Operation or Attico-Antrotomy in 70 Cases.** *J. Laryngol. & Otol.*, 1940, 55: 75.

The problem of the treatment of chronic suppuration from the ear is one which occupies afresh each generation of otologists. If an ear, the subject of a chronic suppurative otitis media, will not clear up with conservative treatment, an operation is necessary, and the aims of this operation may be classed in order of importance: (1) the prevention of intracranial complications; (2) the maintenance of hearing; (3) the reduction and, if possible, the abolition of the otorrhea; and (4) the avoidance of prolonged hospital treatment.

The operation of attico-antrotomy with a meatal flap fulfils these aims, with the exception of the last. There is, of course, a risk of failure (in the author's series about 15 per cent), and this must be accepted. The first aim is fulfilled in both radical and conservative operations. The second can be said to be the particular province of those operations, which spare the middle ear. Exenteration of the contents of the middle ear cannot guarantee a dry ear. In this series with the middle ear intact, there are a number of dry ears, enough at all events to be encouraging. In those cases of this series classed as "moist," the discharge corresponds exactly with that described by certain authorities as occurring after a radical mastoidectomy and dismissed by them as of negligible importance. Finally the worst which can occur is a further operation, and conversion to a mastoid condition requiring radical treatment.

McKenzie suggests the following indications for this operation: (1) if the hearing in the affected ear is "good" or "fair," the middle ear should be spared and an attico-antrotomy done; (2) if the hearing is "poor" and the drum nearly intact with a posterior or attic perforation, the middle ear should be spared; (3) if the hearing is poor, and the drum is absent or not well seen, no decision should be reached until the middle ear is exposed at operation. If, on inspection

of the middle ear, the ossicles are destroyed, only then should a radical mastoid operation be undertaken.

Regarding the question of the flap and the permanent cavity communicating with the meatus, the natural question to ask is, "Why have this at all?" The reasons may be (1), that the posterior meatal wall must be torn at operation in order to gain a view of the attic, and (2) that with adequate and skilled after-treatment, the postaural cavity epithelizes completely. The area is open for inspection at any time, and it is said that the likelihood of a subsequent recurrence of diseases is lessened.

The disadvantages of the flap operation are that the cavity is difficult to manage after operation, and it needs skilled dressing and prolonged treatment, extending from a month to six weeks. If failure occurs, the area of the bridge may scar over, and two cavities are left, one in the attic and middle ear, and one in the mastoid. At the author's hospital a modification of this operation is practiced. With the modified technique, the bone is removed as before, but the flap is not cut. Only a window is cut in the membranous meatus, the end of the postaural pack being brought out through this. The postaural wound is closed entirely. Later, the pack is removed under anesthesia, and not replaced, the cavity being allowed to fill with granulation tissue.

Following operation, 35 per cent of this series of cases were dry, 50 per cent moist, and 15 per cent were unchanged or converted into a mastoid condition. The hearing was good in 34 per cent, fair in 30 per cent, and poor in 29 per cent. The hearing was improved in 57 per cent, unchanged in 28 per cent, and worse in 15 per cent.

NOAH D. FABRICANT, M.D.

## NOSE AND SINUSES

**Smith, A. T.: Osseous Lesions of the Nose and Sinuses, with Special Reference to Hypertrophic Changes and Tumor Formations.** *Arch. Otolaryngol.*, 1940, 31: 289.

In a study of hypertrophic changes and tumor formations in bone lesions of the nose and paranasal sinuses, Smith finds that in contrast to the well established gross and clinical features of the lesions there is a great deal of existing uncertainty as to the pathological interpretation. The majority are treated as osteomas and are thought of as neoplasms. There is considerable confusion as to the term "osteoma." To the pathologist it is a term under which he discusses many forms of overgrowth of bone. To the laryngologist it is a definite clinical entity, for he considers it to be a tumor originating in the bone of the nose and sinuses, encroaching on the cavities, and giving rise to symptoms of deformity, displacement, obstruction, and pressure.

Osteoma as a true neoplasm has not been clearly distinguished from other forms of overgrowth of bone. It appears to be pathologically related to the so-called fibrocystic group of bone lesions. Because of the number of instances in which one finds that it combines the clinical features and histological characteristics of both giant-cell tumor and osteitis fibrosa, the author believes they may be closely allied, and the possibility of a common cause must be considered. Some form of trauma seems to be the most important causative factor. Some other metabolic or nutritional disturbance may be necessary to account for such an abnormal reaction, and further clinical and histological investigation should be carried out to establish the basic nature of these processes. A better understanding of the causative factors may reveal that in the cases in which the lesion cannot be definitely proved to be a true neoplasm, radical surgical intervention with the attendant deformity, in an attempt to eliminate the condition, is not necessary. NOAH D. FABRICANT, M.D.

## PHARYNX

**Townshend, R. H.: The Formation of Passavant's Bar.** *J. Laryngol. & Otol.*, 1940, 55: 154.

In 1869 Passavant described a "cross-roll" which appeared on the posterior pharyngeal wall during articulation in a subject with cleft palate. He claimed that it was essential for normal speech. The question was apparently not discussed further until Wardhill in 1928 announced that his colleague Whillis had discovered the muscle fibers that caused the ridge, and the latter in 1930 gave to his discovery the name of the "palato-pharyngeal sphincter."

Townshend's observations were made on a living subject with a cleft palate and on dissections. He believes that Passavant's bar is obviously produced by the contraction of muscle fibers that arise from the palate in front and run backward horizontally to meet each other behind. These fibers are part of the palatopharyngeus muscle and blend posteriorly with the superior constrictor very soon after arising from the palate. A fascial plane may be present between the upper and anterior parts of the superior constrictor muscle and the palatopharyngeus muscle. This is probably the primitive condition and is tending to disappear. NOAH D. FABRICANT, M.D.

## NECK

**Welti, H., Huguenin, R., and Da Silveira, X. M.: A Contribution to the Study of Chronic Thyroiditis** (Contribution à l'étude des thyroidites chroniques). *Ann. d'endocrinol.*, 1939–1940, 1: 379.

Welti and his associates report 4 cases of chronic thyroiditis of the type described by Hashimoto in 1912 under the name of struma lymphomatosa. This type of chronic thyroiditis has rarely been described in French literature. It differs from sclerosis of the thyroid, which causes few if any symptoms and is often found only at autopsy. It differs also from ligneous thyroiditis, described by Riedel, which is characterized by marked enlargement of the thyroid, often with infiltration of the surrounding tissues.

The type of chronic thyroiditis described by Hashimoto occurs almost exclusively in women; all the authors' patients were women, from forty-nine to fifty-six years of age. The enlargement of the thyroid developed rather rapidly in a gland that had previously been normal; the onset occurred either at the time of or after the menopause. In 3 cases, the thyroid enlargement was accompanied by signs of slight hypothyroidism, i.e., lassitude, apathy, and infiltration of the skin; 2 patients showed a slight rise in temperature—one at the onset of the symptoms, the other later in the course of the disease. The consistency of the thyroid was softer than in Riedel's disease, and there was no involvement of the surrounding tissues. In the first 3 cases, the possibility of cancer was considered, but the mobility of the tumor, the absence of infiltration of the surrounding tissues, and the consistency of the thyroid enlargement were against this diagnosis; in the fourth case, the diagnosis of chronic thyroiditis of the Hashimoto type was based on the findings in the first 3 cases.

In all the authors' cases a total thyroidectomy was done; this operation is justified in this type of thyroiditis as the normal thyroid tissue is either entirely destroyed or only small remnants persist. In all of the cases it was necessary to administer thyroid extract after the thyroidectomy. In the first case, in which no symptoms of hypothyroidism were evident before operation, thyroidectomy was done in two stages; as symptoms of hypothyroidism developed after the first stage, it was necessary to give thyroid extract before as well as after the second stage.

Histological study of the thyroid in these cases showed the lesions typical of struma lymphomatosa, as described by Hashimoto and others, namely, sclerosis, atrophy of the glandular elements, and lymphoid infiltration. The lymphoid infiltration was of two types, either in the form of follicles, sometimes with germinative centers, or in the form of diffuse infiltration between the vesicles of the thyroid; in some areas the infiltrating cells were plasmocytes rather than lymphocytes. These lesions cannot be regarded as absolutely pathognomonic, as similar structures may be observed in "burned out" glands of exophthalmic goiter and in certain cases of thyroiditis of the Riedel type. The diagnosis of "struma lymphomatosa" depends upon the clinical picture as well as the histological findings. The essential clinical characteristics are: the occurrence in women after the menopause, the absence of hyperthyroidism, and, on the contrary, a tendency toward hypothyroidism. ALICE M. MEYERS.

**Wilson W. D., and Mayo, C. W.: A Histological Study of the Thyroid of Exophthalmic Goiter at Intervals During the Administration of Iodine.** *Surgery*, 1940, 7: 325.

One hundred cases in which exophthalmic goiter was treated with iodine and operated upon in stages have been studied histologically with a control group of 10 cases in which Lugol's solution was not given. The following conclusions were drawn:

1. It seems that in this series there was evidence of a tendency toward decreased activity or histological involution in the thyroid glands of the majority of the patients who were treated for long intervals by iodine in whom a change was noted, while there was some histological evidence of increased activity in the second stage in the glands of most of those treated for shorter periods in whom a change was seen.

2. There seems to be histological evidence of an increase in activity of the thyroid gland in exophthalmic goiter during the winter months.

3. The amount of colloid varies inversely with the "activity" of the thyroid gland.

4. The amount of regenerative hyperplasia in the gland varies directly with the "activity" of the thyroid gland.

5. That the histological observations made in this study are valid is suggested by the computation and co-ordination of the ratio of the basal metabolic rate to the weight of the thyroid substance removed.

**Dargent, M., and Berard, M.: Extensive Operation for Carcinoma of the Thyroid Gland** (De l'intervention élargie dans le cancer du corps thyroïde). *J. de chir.*, 1940, 55: 131.

More than 100 cases of carcinoma of the thyroid gland were studied and form the basis for this paper. Thyroid cancer is divided into two large groups, namely (1) cancers which are of low-grade malignancy; and (2) cancers which are of high-grade malignancy.

Thyroid cancers of limited malignancy may be removed radically even when complicated by bony metastases because after the removal of the primary tumor the patients live for ten years or more. The same type of patients in whom malignancy is found at the time of operation, but upon whom radical operation is not carried out, live but a limited time because of the extensive growth of the local cancer. The operation consists essentially of a very complete removal of the thyroid gland including all adenomas. The extension of the cancerous process to the ganglions, muscles, and aponeuroses of the neck, and the internal jugular vein is a bad omen because these parts act as proliferating centers for further extensions. The finding of these extensions suggested the very extensive type of operation which the authors recommend. Roentgen therapy is only moderately effective in the low-grade cancer of the thyroid, which is rather resistant to irradiation.

The authors suggest and practice the removal of the sternomastoid muscle and its superficial aponeurosis, the omohyoid and infrahyoid muscles and the middle aponeurosis, the internal jugular vein, the superior thyroid artery, and all of the tumor in one mass.

In the first case the patient presented an atypical epithelioma, and extensive removal of the tumor, blood vessels, and muscles was carried out. In the second case a papillary epithelioma was found and extensive removal of the tumor, muscles, ganglions,

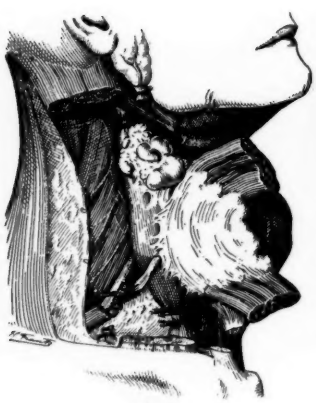
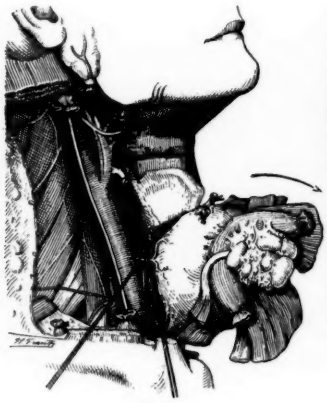


Fig. 1.



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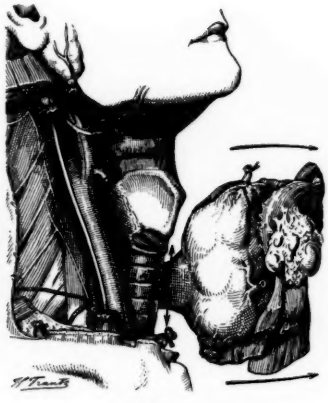


Fig. 3.

Fig. 1. Section of the inferior head of the omohyoid muscle. Resection of the internal jugular vein and of the ganglion mass.

Fig. 2. Dissection of the recurrent nerve and its ganglion chain. Ligation and section of the inferior thyroid artery. Separation of the artery and the nerve.

Fig. 3. Freeing of the trachea. Hemostasis of the inferior and middle inferior thyroid veins. The healthy isthmus is sectioned. Hemostatic suture of the section. (The operation is followed by the removal of the opposite lobe and immediate grafting of a parathyroid body in case of doubt.)

and blood vessels was carried out. Both patients were operated upon in July, 1939, and are living and well.

*Operative technique.* The operation is carried out under local anesthesia. A transverse incision runs from the center of the tumor to the anterior portion of the sternomastoid muscle of the opposite side. The longitudinal incision runs from the mastoid process to the clavicle across the center of the tumor. The external jugular vein is doubly ligated and the sternocleidomastoid muscle is completely removed in the course of this dissection. The inferior head of the omohyoid muscle and of the middle cervical aponeurosis is excised. The scalenus anterior and the phrenic nerves are seen as well as the brachial plexus. The internal jugular vein is tied very high under the posterior belly of the digastric muscle. The descending branches of the hypoglossal nerve are cut. The resection of the internal jugular vein is carried out in its entirety as far as possible. The superior thyroid artery is next isolated and removed. The bifurcation of the carotids is explored and excess tissue removed. The infrahyoid muscles are removed in their entirety. The laryngotracheal groove is next dissected clean. The thyroid isthmus is divided well on the healthy side of the trachea. There have been no cases in which the tumor invaded the common carotid artery.

This extensive operation is suggested for all malignancies of the thyroid which have extended to any surrounding structures. It is not indicated when extensive metastases or extensions are present, especially in recurrence. It should be carried out even when there are no signs of invasion of the ganglions. The contraindications are as follows: extreme cachexia and wide-spread metastases; extension to the trachea and esophagus; and tumors which involve the connective-tissue, as this type does not respond well to large mass excision. When there are marked extension and adhesions to the trachea or esophagus, operation is contraindicated and roentgenotherapy is indicated.

An extensive operation is proposed (the end-results of which are not yet known as the cases have not been carried along far enough to anticipate them) because it is known that the Wertheim massive removal in carcinoma of the cervix gives good results.

RICHARD J. BENNETT, JR., M.D.

**Miller, M. V.: Edema of the Larynx: A Study of the Loose Areolar Tissues of the Larynx.** *Arch. Otolaryngol.*, 1940, 31: 256.

Because information on edema of the larynx was scant and unsatisfactory, Miller decided to undertake his own investigation. While experiments on the cadaver cannot exactly reproduce what occurs in the living subject, they can undoubtedly give a rather accurate idea of the extent to which edema of the larynx may extend. They seem to indicate that edema may be localized between two adjacent condensations of fibrous tissue. Certain chemical or physiological effects of the fluids may develop in these tissues in disease which might decrease the efficiency of these condensations as barriers to the spread of involvement, as compared with their efficiency in checking the spread of the fluid in these injections. Certain types of edematous fluids may spread more rapidly than others because a difference in the protein content affects the diffusibility. Various factors such as these make it difficult to

evaluate clearly the clinical importance of these particular findings.

Localized edema is known, however, to occur in various parts of the larynx, and many times in areas which might be limited by the barriers here described. So far as the author has been able to determine, no clinician has observed unilateral edema over the esophageal surface of the cricoid. Whether this is because it has been hidden by edema over the arytenoid areas is not known, but it seems likely, as involvement of this area would almost surely be accompanied by edema over the arytenoid area and the aryepiglottic fold of that side.

These experiments indicate also that if the edema involved only the valleculæ and the anterior surface of the epiglottis, there would be little interference with breathing and probably few symptoms other than a sensation of a mass in the throat. It is possible, however, that with the broadening of the surface of the epiglottis and the consequent interference with close approximation of the aryepiglottic folds there might be some difficulty in completely closing the airway when swallowing and fluids might trickle down into the larynx. Such a localization might follow involvement of the lingual tonsil or ulcerations of the epiglottis.

The results also indicate that with infections of the tonsil or the lateral pharyngeal wall, when edema arises it may extend downward into the piriform sinus and from there extend into the aryepiglottic fold. Edema of one aryepiglottic fold might cause some respiratory difficulty but would not cause asphyxia; however, if both should become involved the situation would become acute. It appears that in mild conditions the fold only would be invaded, but it seems sure that if there were much swelling of the structure the fluid would almost certainly have to extend down over the esophageal surface of the cricoid and also invade the deeper tissues on the interior of the larynx. If this involved only one side there would still be breathing space, but if both were involved there would be asphyxia.

The findings seem to emphasize the need for careful watching in any case in which edema has developed or may develop, as the fluid may travel fast and far and when there is swelling of the upper structures one cannot see how rapidly the obstruction is developing below. One should always be prepared for emergency tracheotomy at the first signs indicating acute asphyxia.

NOAH D. FABRICANT, M.D.

**Coutard, H.: The Present Conception of the Treatment of Cancer of the Larynx.** *Radiology*, 1940, 34: 136.

The five-year results of roentgen therapy of cancer of the larynx reported in 1932 are not greatly superior to those of 1921. The progress was only in some details. Differentiated cancers infiltrating the muscles and intimately united with them, immobilizing the muscles and immobilized by them, generally remained incurable by this method of treatment.

We now have a better knowledge of the chronological involution of cancer of the larynx, and of the chronological steps necessary for its treatment. For a long time we have been influenced by the fact that the undifferentiated forms of this disease disappear with extreme rapidity, whereas the differentiated forms disappear only after three or four months; but the dose which provokes the disappearance of the latter is approximately the same as that which causes the disappearance of the former.

The transportation of the cancericidal dose to the neoplastic cells through the normal tissues, i.e., the distribution in space, has been considered for many years the principal problem in roentgen therapy. Yet this is only the physical part of the problem—the part which should be simplified until we need not consider it any longer. The essential problem is the distribution of time, and physiological repartition.

A simplification of the use of high voltage has been accomplished by the use of a single field with a regular and daily decrease in the surface area and with a regular and daily increase in the dose. The use of this technique increases considerably the precision of treatment and its efficacy, the necessary doses are reduced, and the cancers appear to be more radiosensitive.

In differentiated cancer of the larynx, pharynx, and buccal cavity, the results of the new method seem better than those obtained heretofore.

JOSEPH K. NARAT, M.D.

# SURGERY OF THE NERVOUS SYSTEM

## BRAIN AND ITS COVERINGS; CRANIAL NERVES

**Keller, C. J.: The Regulation of the Blood Circulation of the Brain** (Die Regelung der Blutversorgung des Gehirns). *Ztschr. f. Neur.*, 1939, 167: 281.

The methodical study of the regulation of the blood circulation of the brain is very difficult. Recently the following have been added as new methods of study: the observation of the width of the vessels through a window in the skull (Forbes); the thermoelectric measurement (Gibbs); the diathermothermal circuit timer (Rein); and the observation of the circulation of the isolated head (Bonchaeu and Jourdan). The cerebral arteries are by no means end-arteries as Cohnheim assumed; for numerous arterio-arterial and arteriovenous anastomoses exist. The circulation bed of the thyroid gland is arranged in a parallel fashion to that of the head, and the circulation of the external carotid artery is arranged in a parallel manner to that of the brain. Intracranially, the same is true of the circulation of the dura mater and that of the choroid plexus. A considerable short circuit exists between the cerebral circulation and the external carotid artery through the ophthalmic and the angularis arteries. It is because of this very fact that the regulation of the cerebral circulation, independently from the general circulation, becomes understandable. The aim of the cerebral circulation is to supply blood and nourishment to the central nervous system and its branches.

The circulation of the brain is a comparatively very large one—1 liter of blood per minute—15 per cent of the total minute volume of the heart. The central nervous system is much more sensitive to anemias and hyperemias than, for example, the skin and the musculature. The former is also more protected by means of the bony skull; however, this alone would not be sufficient. For over a century the theory of passive cerebral circulation remained firm. Of course, the general blood pressure and the cerebral circulation have something in common with each other, but if this were always true, then every small circulatory shock would bring about severe or even irreparable disturbances of function in the brain. However, this is not the case. If one, for instance, should voluntarily produce histamine shock, a drop in the blood pressure will develop in the aorta and in the circle of Willis, but in spite of this, the congestion of the brain circulation increases tremendously and reaches its maximum just at the height of the drop in blood pressure. When the general blood pressure again increases, the congestion of the brain circulation drops markedly. However, this is followed by a secondary increase in the blood volume in the internal carotid artery which is independent of the general as well as the intracerebral blood pressure. This fact speaks unequivocally for the existence of a local autoregulatory mechanism which probably is of a neurogenic character.

These results of animal experimentation may be applied also to man. It is by no means correct to put the blood pressure in the foreground. There is no circulation which is passively regulated by pressure alone. Of foremost importance is the automatic heart action. To be sure, the circulation of the resting brain follows the spontaneous blood-pressure deviations. Nevertheless, the hemodynamics of the cerebral circulation have certain peculiarities. The arterial pulse wave produces a change of space intracerebrally, which primarily acts as a compression of the venous system. In general, under normal circumstances, the same amount of blood is brought to the brain as is carried away. It is also a fact that by gradual increase in the intracerebral pressure, as a result of a decrease in the intracranial space, a gradual diminution occurs in the amount of blood brought to the brain; this is at first accompanied by a short temporary increase in the venous outflow. As soon as the increased pressure undergoes a change in any manner, whether with relation to time or quantity, complicated regulatory mechanisms go into action. The ability of the brain circulation to be influenced by nervous factors is still the object of greatest disagreement. The fact that most of the cerebral vessels possess nerves has been proved; the effects of physical influences, such as increased activity, warmth, cold, and extracerebral pressure, are more clearly demonstrated upon the veins of the neck. Certain it is, however, that the sympathetic system exercises a regulating influence upon the cerebral circulation. With respect to the vagus influence, one can well say that its stimulation results in a vasodilatation and an increase in the blood flow of the brain. Opinions still vary very widely as to whether the nervous influences upon the cerebral circulation are the result of direct or reflex processes.

Of the greatest interest in this respect are the reflexogenic zones of the external and internal carotid arteries. Rein found that after occluding the common carotid artery an increase occurs in the circulatory volume, which amounts up to as much as 100 per cent, in the contralateral vessel. M. and D. Schneider found that this could not possibly be due to a passive process, since this phenomenon did not occur in a denervated organ. They showed further that when branches of the external carotid artery were tied off, the compensatory increase in the circulatory volume of the internal carotid artery failed to develop if the vessel were tied beyond the origin of the middle meningeal artery. This evidently was due to the meningeal reflex which has the function of being a regulatory mechanism to prevent a threatening cerebral anemia. The influence of the brain circulation through extracerebral vascular and nervous channels is, to be sure, still a very mooted subject.

In this respect there stand, above all, the pressor receptors, which ordinarily exert an extremely forceful influence upon the autoregulation of the circulation. Keller, however, does not doubt the influence of these pressor receptors also upon the cerebral circulation, no matter how minimal this influence may be.

Just as in the coronary circulation, one cannot underestimate the importance of the active reflex regulation of the cerebral circulation by the sinus nerves in the presence of functional pathological conditions. These processes, however, become complicated because of the relationship of the cerebral with the thyroid circulation; the latter, as a rule, behaves in an opposite manner to that of the cerebral circulation, as far as pressure regulatory processes are concerned. This fact is of importance, especially in marked pressure elevations in the regions of the head and neck. For the brain, therefore, a circulatory short circuit which stands under the control of the sinus nerves may be created either by way of the direct internal-external (carotid) anastomosis or by way of the thyroid circulation. Unfortunately, however, we know nothing, physiologically speaking, either about the regulatory mechanisms which act only intracerebrally or about the nervous mechanisms which control them.

The nervous influence upon the regulation of the cerebral circulation undoubtedly becomes of secondary importance to the passive phenomena as well as to the heart action. Ordinarily, however, this is the case only when great changes in the circulation take place. In the case of local and pathological conditions, however, it is quite a different matter. The following example will elucidate these statements: in the case of ophthalmic hemicrania the retinal vessels on the side of the lesion are narrowed to a maximum degree. However, if one injects intravenously 0.3 mgm. of gynergen, the retinal vessels become widened and the attack ceases. The influence of chemical substances upon the cerebral circulation is striking. This is true particularly of the nitrites, and, in the order named, caffeine, lobelin, camphor, cardialzol, sympatol, and ephedrine; acetylcholine, the vagus-like substance, also causes a widening of the cerebral vessels in spite of the bradycardia and drop in the blood pressure.

The action of adrenalin upon the cerebral vessels is extremely controversial. However, every brain surgeon knows that the local use of adrenalin causes a vasoconstriction and that the injection of adrenalin into the carotid artery results in an almost complete throttling of the brain circulation. It is only after the adrenalin begins to take effect in the general circulation that this throttling action upon the brain circulation starts to wear off. The most important, however, are the effects of oxygen and carbon dioxide. The circulatory volume of the brain begins to show an increase under concentrations of carbon dioxide, which do not lead to a general rise in the blood pressure. Carbon dioxide is the most important substance for the regulation of the blood in the brain. This substance, however, produces a severe disturbance of the entire circulation, by way of the central nervous system, by causing a contraction of the muscle, splanchnic, and kidney blood vessels (Rein). This process supersedes almost all other nervous regulatory phenomena. Thus the cerebral circulation acts upon the general circulation in so far as the former becomes the bearer and distributor of this reaction.

(Franz). Harry A. Salzmann, M.D.

**Ducuing, J., D'Harcourt, J., Griño, A., and Folch, A.: General Principles in the Treatment of Fresh Craniocerebral Injuries of Warfare** (Principes généraux du traitement des plaies cranio-encéphaliques récentes par projectiles de guerre). *Rev. de chir.*, Par., 1939, 58: 625.

This article, most *à propos* at this time of a new European conflict, attempts to cover in a general and rather telescopic manner all the principles of treatment and after-care of fresh craniocerebral injuries received in battle. It is intended to act as a ready guide to young surgeons and general surgeons whose main experience has not been in the field of trauma to the nervous system. It is written somewhat in the manner of an army medical manual.

The observations by the authors on the cranial injuries seen in the World War and in the recent Spanish war have made them conscious of many errors of treatment. Some of these were the result of inadequate physical equipment for the care of the wounded, lack of knowledge of the nature of intracranial hypertension, too frequent lumbar punctures, too great use of general anesthetics, insufficient respect for the possibility of infection, loss of control of the patient too soon after operation, and many other equally serious factors. The authors go to some length in enumerating the general characteristics of the cranial injuries typical of warfare, such as the presence of multiple cranial openings (such patients usually have other bodily injuries as well); the various possibilities as to the loss of skin, bone, dura, and cerebral tissue; the types of injury to the ventricles and large venous sinuses; and, perhaps most important of all, they bring out the fact that the wounds are always septic.

They are particularly concerned with the treatment of post-traumatic and postoperative cerebral edema, for they believe that except for infection, this is the factor most likely to cause the death of the wounded. They use lumbar puncture cautiously and realize its value, but they depend mainly upon hypertonic solutions administered intravenously to bring about dehydration through physiological means.

The authors point out not only that the surgeon must have adequate instruments and other equipment with which to work, but also that special care in transportation (the wounded should not be transported far to a hospital), early operation, and long-continued postoperative observation by the surgeon are principles which must be faithfully followed. The operation must not be hurried; shaving, cleansing,

and débridement must be done very carefully; hemorrhage and shock must receive primary consideration; the dura mater must be preserved and kept intact if that is at all possible; and the wounds should be closed without drainage. The ensuing cerebral edema will allow no relaxation of nursing care, which must be intelligent, and the wound must be considered potentially still infected until the patient has completely recovered. The authors have recently found sulfanilamide of great benefit in the treatment of septic craniocerebral injuries. JOHN MARTIN, M.D.

**Bull, J. W. D.: The Roentgenological Diagnosis of Chronic Subdural Hematoma.** *Proc. Roy. Soc. Med.*, Lond., 1940, 33: 203.

Any contribution to the accurate diagnosis of chronic subdural hematoma, which is frequently a perplexing lesion, is always welcome, and this article seems definitely to establish certain criteria which should aid in the roentgenological diagnosis of this lesion.

In a series of 26 cases of subdural hematoma which were studied until recovery occurred and were completely analyzed in the Roentgen Department of the Royal Serafimer Hospital of Stockholm, Bull found on plain films that (1) no fracture was seen in any case; (2) signs of increased intracranial pressure were found in only 2 cases (widening of the suture lines in a patient of twenty-eight years, and thinning of the dorsum sellæ); (3) no gross bone changes or abnormal vascularization of the bones were seen; (4) the pineal gland, found calcified in 8 cases, was displaced laterally in but 2 cases; (5) a calcified chorioidal plexus, seen once, was not displaced; (6) calcification of the hematoma was not found; (7) the skull shadow on the side of the lesion was in no case denser than on the opposite side. Calcification, if present, would be pathognomonic, but it is more usual in the infant than in the adult hematoma.

Fig. 1.

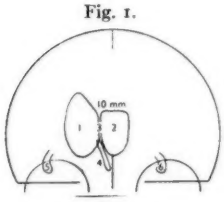
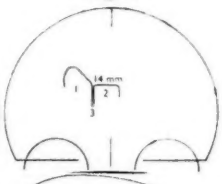



Fig. 2.



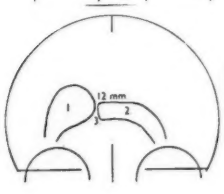




Fig. 3.

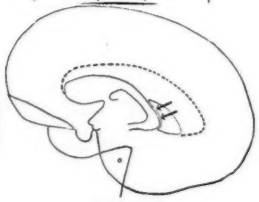



Fig. 4.

Fig. 1. Mean drawing in supine position. Note: 10 mm. shift of septum. Medial displacement of 6.

Fig. 2. Mean drawing in sitting position. Note: 14 mm. shift of septum.

Fig. 3. Mean drawing in prone position. Note: 12 mm. shift of septum.

Fig. 4. Typical lateral drawing. Note: Falx pressure; contralateral ventricle dotted.

KEY TO FIGS. 1, 2, and 3.

1. Contralateral ventricle: dilated, lateral roof high.
2. Homolateral ventricle: not dilated, roof flat.
3. Septum pellucidum: shifted but vertical.
4. Anterior part of third ventricle: upper part shifted laterally; forms angle with septum pellucidum.
5. Contralateral temporal horn: normal position.
6. Homolateral temporal horn: medial shift.

Pneumo-encephalography, usually encephalography by cisternal puncture, was found to be of great aid in the diagnosis of the hematoma. Of the total series, 18 cases were studied by air injections, of which 12 showed a remarkable similarity, noted particularly in the anteroposterior position. The salient changes found were: (1) marked shift of the septum pellucidum without much angulation; (2) shift and angulation of the anterior portion of the third ventricle; (3) an angulation between the septum pellucidum and the third ventricle; (4) contralateral hydrocephalus; (5) slight or no dilatation of the lateral ventricle on the side of the hematoma; (6) flattening of the roof of the ipsilateral ventricle; (7) elevation of the roof on the contralateral side; and (8) varying medial displacement of the temporal horn on the affected side. When the films were made in the sitting position, (9) a more marked flattening of the roof of the lateral ventricle on the affected side was seen, and (10) there was a greater displacement of the septum pellucidum. These 12 cases, superimposed to form composite figures, are represented in Figures 1, 2, 3, and 4.

Arteriography, not frequently used nor particularly condoned by the author, showed no contrast medium in the hematoma. Two cases of bilateral hematoma occurred in this series.

The author believes that, although no x-ray findings of hematoma are absolutely pathognomonic, the suggestion of such a lesion by the x-rays may lead to diagnostic burr holes, and thus avoid the more serious and often unnecessary elevation of a flap. JOHN MARTIN, M.D.

**Pisani, D., and Scalori, G.: Rhinopharyngeal Cancer with Propagation into the Cerebral Subarachnoid Spaces** (Cancro rino-faringeo con propagazione agli spazi sub-aracnoidei cerebrali). *Settimana med.*, 1940, 28: 1.

The neurological picture of tumors of the rhinopharynx is usually characterized by the unilateral or bilateral involvement of many cranial nerves, bony changes in the base of the skull which are demonstrable with x-rays, the absence of signs of increased intracranial pressure, and the absence of motor or sensory involvement of the extremities. Occasionally, however, the x-ray findings may be negative, and signs of increased intracranial pressure and motor and sensory involvement of the limbs are present.

The case presented is that of a forty-one-year-old male with diffuse basal-cell carcinoma of the rhinopharynx. The onset was characterized by a sense of obstruction in the nose, and soon thereafter of headache and vomiting, which were attributed to increased intracranial pressure. Following this there occurred paralysis of the fifth to the twelfth cranial nerves on the right, and of the sixth to the twelfth on the left. Many cancer cells were found in the spinal fluid. This finding indicated that the tumor had penetrated into the cerebral subarachnoid spaces, which is an unusual occurrence, as ordinarily these tumors do not pierce the dura.

DAVID IMPASTATO, M.D.

**Kos, C. M.: Tumor of the Facial Nerve Within the Mastoid Bone.** *Ann. Otol., Rhinol. & Laryngol.*, 1940, 49: 151.

The second recorded instance of a tumor of the facial nerve within the mastoid bone furnishes the text of this brief article. The tumor was discovered during the course of dissection of 400 mastoid cadaver specimens, and it lay in the facial canal in the angle formed by the posterior wall of the external auditory meatus and the sigmoid sinus, on a level with the facial nerve. Parts of the tumor were fused to the nerve, and parts of it were attached to the adventitia of the sigmoid sinus.

Cytological fixation was poor and microscopic study was correspondingly difficult. Cystic or venous spaces, the walls of which were hyalinized, were quite numerous. Bundles and whorls of long, wavy reticular and collagenous fibers surrounded the long axis of the facial nerve, and the mass appeared to be mainly of connective tissue. Its general classification would seem to be that of neurofibroma.

JOHN MARTIN, M.D.

## SPINAL CORD AND ITS COVERINGS

**Saunders, J. B. deC. M., and Inman, V. T.: The Pathology of the Intervertebral Disc.** *Arch. Surg.*, 1940, 40: 389.

The intervertebral disc may be involved by degeneration, trauma, infection, and neoplasm. Traumatic rupture of the cartilage plate occurs in conjunction with compression fracture of the vertebral body. An important variety of trauma to the cartilage plate is that associated with marginal fracture of the vertebral body. These chip fractures are usually anterior, and are followed by collapse and thinning of the disc. Rupture of the cartilage plate occurs secondary to loss of support by the spongiosa of the vertebral body. The most common form is that associated with senile osteoporosis of the spine. Similar rupture of the cartilage plate follows loss of bony support due to invasion of the vertebral body by infection or tumor.

Degeneration may occur as early as the third decade, or before, if the integrity of the disc has been interfered with by trauma or congenital defects. The earliest change is an exaggeration in the size of the nucleus pulposus with an extensive development of cavitation. Later, breakdown in the fibrillary structure and the dissolution of the cellular elements occur until the whole nucleus is reduced to an amorphous mushy mass. In this mass quite rarely calcium salts are deposited. By this time minor defects and erosions of the confining cartilage plates have appeared, which may rupture and lead to the escape of nuclear material. Extruded nuclear material shows a marked tendency to become transformed at its periphery into cartilage, pseudocartilage, or bone.

The annulus fibrosus likewise shows degenerative changes. With the onset of degeneration the inner layers emerge into the expanding nucleus until little more than a ring of the original tissue persists. During this process the lamellæ become swollen and areas of necrosis and vascularization appear. The fibrous bundles may separate and produce concentric fissures. These concentric fissures are most frequently anterior and occur most characteristically in kyphosis of old age. The radial fissures are most often found dorsally, and through them nuclear material may herniate into the vertebral canal.

Dorsal protrusions, displacements, or herniations of the disc tissue may cause pressure on the contents of the neural canal. Extradural tumors, variously termed chondromas, fibromas, chondrochondromas, exostoses, and enchondroses, are now clearly recognized as being due to dorsal displacement of disc tissue.

Infections and tumors rarely involve the discs primarily or secondarily. In acute destructive processes such as staphylococcic osteomyelitis, the disc may be completely destroyed. In tuberculosis the disc is nearly always involved secondarily. The disc may be also involved in syphilitic spondylitis, syphilitic osteo-arthropathy, and in syringomyelia. Primary tumors of the disc, the chondromas, are rare.

Adolescent kyphosis is a condition of which the cause is obscure. Clinically it is characterized by a rigid rounded kyphos, centered usually between the seventh and tenth thoracic vertebræ. The kyphos is rarely discernible before the age of ten; the onset is most frequent between the ages of fifteen and seventeen years. The patients are nearly always healthy with excellent musculature. Pain is an inconstant complaint and is usually in the nature of an ache on exertion. The x-ray pictures are distinctive. The first deviation from the normal is an irregularity of the subchondral bone at the superior and inferior surfaces of the vertebral bodies. These surfaces, instead of appearing as a thin, smooth, continuous distinct line, becomes irregular and broken. The disc is always narrowed. In most cases sizable herniations of the nuclear material into the spongiosa are indicated by sclerosis of the adjacent bones. In older lesions the abnormal transmission of weight from vertebra to vertebra in the region of the kyphos leads to wedging of the vertebral bodies, sclerosis of the anterior portions of the superior and inferior surfaces of the vertebræ, and osteophyte formation.

Senile kyphosis is due to a special type of destruction of the disc. The characteristic feature is the spinal curvature, which appears usually in late life, and develops rapidly as an exaggeration of the physiological thoracic curve. The curvature is most marked in the upper thoracic spine and may progress to a high degree. Post-mortem studies on senile kyphosis indicate that the essential pathological process is a pressure necrosis of the anterior portion of the intervertebral discs.

Spondylitis deformans is the outcome of degeneration of the intervertebral discs. This degeneration is usually generalized throughout the vertebral column. There is a dissolution with loss of substance in the nucleus pulposus, followed by relaxation and protrusion of the annulus about the periphery. This leads to lateral shifting of the bodies.

Ankylosing spondylitis is considered by more recent investigators as rheumatoid arthritis involving primarily the small articulations of the spinal column. There follows smooth ossification of the anterior longitudinal ligament and of the outer layers of the annulus without formation of osteophytes. The discs disappear to a greater or lesser extent and are replaced by bone. DAVID J. IMPASTATO, M.D.

**Hampton, A. O.: Iodized Oil Myelography: Use in the Diagnosis of Rupture of the Intervertebral Disc into the Spinal Canal.** *Arch. Surg.*, 1940, 40: 444.

With an accuracy of 93 per cent in 133 cases at the Massachusetts General Hospital, Hampton has used iodized oil intrathecally in the diagnosis of ruptured intervertebral disc. The failures, not due to any fault of the myelography, proved to be such lesions as a dilated arachnoidal vein, a fractured pedicle, a small osteoma, and 2 cases of thickened ligamentum flavum. Hampton favors the use of oil rather than air in myelography, believing that the technique for the use of the latter and the interpretation of the films is so poorly worked out that an error of 50 per cent may be expected. He recognizes, however, that oil in the subarachnoidal spaces is a foreign body and may act as such to produce disturbing or dangerous effects.

A fairly detailed account of the handling of the patient on the x-ray table in the examination of the lumbar spine is given. The author warns that care should be taken to select fresh oil, since old or deteriorated oil, dark of color, may cause severe though transient reactions. From 4 to 5 c.cm. of oil are necessary, smaller amounts being inadequate unless there is a frank block of the cerebrospinal fluid due to a ruptured disc, which is not often found. In discussing the technique for lumbar fluoroscopy, the author points out that the oil must not be allowed to "bead" or string out; that a suspicious filling defect must be constant on several films to be of any real significance; that a symmetrical, smooth, hour-glass shadow is rarely due to a ruptured disc; and that since the first sacral nerve crosses the fifth lumbar disc outside of the shadow of the iodized oil, it is possible for a rupture of the fifth lumbar disc to press on the first sacral root and yet not be demonstrated by oil myelography. Several photographs illustrate typical myelographic findings in the presence of ruptured intervertebral discs in the lumbar spine.

JOHN MARTIN, M.D.

**Love, J. G., and Walsh, M. N.: Intraspinal Protrusion of the Intervertebral Discs.** *Arch. Surg.*, 1940, 40: 454.

The authors say it has been only within the last few years that a clinical diagnosis could be made of posterior protrusion of an intervertebral disc into the spinal canal, with subsequent compression of the spinal cord or of one or more nerve roots, and yet today it is a diagnosis that can be made in a very high percentage of cases by any up-to-date physician.

The authors emphasize the fact that they strongly favor and urge a trial period of so-called conservative treatment, unless there is gross evidence of damage to the central nervous system, before the undertaking of neurosurgical methods for the relief of pain in the neck, shoulders, back, or lower extremities. A period of observation with conservative treatment will indicate to the careful observer, in many cases, that there is an underlying lesion of the spinal cord or of a nerve root, which must be attacked centrally.

They are convinced that the intervertebral fibrocartilaginous discs protrude posteriorly into the spinal canal as the result of unusual stress or strain applied to the vertebral column. This stress may be the result of a single outstanding injury or it may be the result of repeated injuries of varying degrees of severity.

In an analysis of 500 consecutive cases in which operation was performed at the Mayo Clinic for protrusion of one or more intervertebral discs, the authors have learned that 58 per cent of the patients gave a history of a specific injury to the back. Approximately 96 per cent of the 500 patients seen had lumbar protrusions. This is a very important fact, the authors say, for it helps to make an otherwise extremely complicated problem comparatively easy to solve.

The most common symptoms and signs, and those of greatest value in arriving at a clinical diagnosis of protrusion of a lumbar disc were unilateral sciatic pain in 78 per cent of the cases, and bilateral sciatic pain in 16 per cent. In the other 6 per cent, backache alone, or extension of pain other than along the course of the sciatic nerve, occurred.

The three neurological signs which continue to be the most helpful in the diagnosis of lumbar-disc protrusions are Lasègue's sign, positive in 84 per cent of cases; sciatic tenderness, positive in 64 per cent; and diminution or absence of the Achilles reflex on the side of the pain, in 60 per cent.

The most important finding in the analysis of the spinal fluid in such cases is the total protein content of the spinal fluid. [In the entire series, 40 per cent of the patients had less than 40 mgm. of total protein

per 100 c.cm. of spinal fluid in the specimen submitted for analysis.]

When a diagnosis of protruded intervertebral disc is made and the surgical method of treatment is decided on, the operation should be performed by someone familiar with intraspinal surgery.

The anesthetic agent of choice is ether, administered by the open drop method.

The operative exposure of a protruded disc should be as accurate and as limited as possible; however, adequate room for the removal of all fragments is essential. The articular facets and pedicles should be preserved. No more bone should be removed than is absolutely essential for visualization and removal of the protruded portion of the involved disc. Whenever possible, a modified type of laminectomy should be employed; that is, instead of removing 2 or 3 pairs of laminæ, the removal of a portion of one pair should suffice in most cases. At times, because of great thickening of the ligamentum flavum and a listing of the patient away from the side of the protrusion, the lesion can be removed without the removal of any bone. It has been possible to remove the protruded disc in more than 20 cases without the removal of any bone from the spinal column. Theoretically, the less bone removed, the stronger the back will be postoperatively, and if at any subsequent time fusion should be required, it can be done with greater ease if none of the spinous processes or laminæ has been removed.

The pathological changes observed in cases of so-called hypertrophy of the ligamentum flavum are as follows:

Grossly, the affected ligaments are thicker than normal; they measure from 4 to 6 mm. in cross section as against an established normal of from 2 to 5 mm. The cut surface, instead of being homogenously yellow, reveals in a typical case white bands running throughout. Microscopically, the changes, seen best with special stains for elastic tissue, are as follows: 1. Fragmentation, usually longitudinal, of the elastic tissue fibrils; the ends of these frayed fibrils often appear shriveled. 2. Replacement of damaged fibrils by a more primitive type of mesoderm, namely, fibrous connective tissue. The latter, in many instances, is present in the form of wide bands that run throughout the length of the affected ligament. 3. Blood vessels are few in number and those present are small in caliber as a result of hyaline substance which is deposited within their walls and which replaces the muscularis. This finding leads one, the authors say, to wonder whether vascular damage as a result of trauma may not explain the other changes observed. In 3 "normal" controls studied to date, vascular changes were not noted and the ligaments had none of the alterations noted microscopically.

**Macey, H. B.: Clinical Aspects of Protruded Intervertebral Disc.** *Arch. Surg.*, 1940, 40: 433.

This is an attempt to present the findings noted on orthopedic examination and, to a lesser extent, on neurological examination in 100 cases in which a posterior protrusion of an intervertebral disc was of apparent significance in producing the patient's symptoms. It is believed that this syndrome presents sufficient clinical evidence in the history and the examination to arouse suspicion of a posteriorly protruded disc in practically all cases seen, the majority of which can be diagnosed on a clinical history and examination alone. However, roentgenological examination should probably be carried out on all patients to determine the location of the protrusion or protrusions. Also, there is a group of cases encountered in the quiescent period in which a roentgenological examination is necessary for confirmation of a suspected lesion. There is still a third group with the usual clinical findings and history in which the results of the roentgenological examination are negative, and these must be considered for an exploratory examination.

In 23 of 100 cases studied, there was a history of injury severe enough to initiate symptoms unquestionably attributable to the injury. It was of interest to note that in 17 of the 23 cases the injury was sustained with the spinal column in a position of flexion and torsion; in the other 6 the posture was not known. In 9 cases of the group studied, there was a history of many years of backache without known injury to produce the symptoms. In all of these cases the onset of the sciatic pain occurred while the patient was doing some type of work which required standing with the spinal column in a position of flexion, such as shoveling snow and pitching hay, following which the pain was of a persistent nature. In 68 cases of the series, the patients did not associate the condition with any injury of sufficient magnitude to produce onset of the symptoms. From the data obtained it is difficult to draw any definite conclusion other than that the syndrome may produce the following: (1) recurrent backache and recurrent sciatic pain, (2) continuous backache and recurrent sciatic pain, (3) continuous backache and continuous sciatic pain, (4) continuous sciatic pain without backache, or (5) recurrent sciatic pain without backache.

From the pathological anatomy one must conclude that the protrusion results from an injury or injuries, or possibly from disease, although so far as is known by the author the latter has not been reported. The impression one gets in reviewing these cases is that injuries are the basis of all posterior protrusions, but that the degree of the injury or multiple injuries determines the clinical history and the clinical course of the syndrome.

With a severe injury there may be an acute rupture of the posterior annulus and a corresponding bulge of sufficient degree and so placed that continuous symptoms are produced. There may be a spontaneous rupture from an apparently trivial injury in a previously damaged annulus. Also, there is some mechanism whereby the pressure from this posterior protrusion on the nerve root is released, and remissions occur between the attacks. The nature of this mechanism leads to much speculation.

In 50 of the group of 100 cases, there was a unilateral limited ability to perform the straight leg raising test; in 24 it was limited bilaterally, and in 26 the patients were considered normal in this respect. The characteristic position of the spinal column in the more acute cases was a list to the unaffected side with a scoliosis of the lumbar vertebræ. This was noted in 33 of the 100 cases seen. In only 5 cases was there a list to the affected side. In 24 cases the posture was good, while in 21 cases no mention of posture was made and one would assume that it was good.

In 50 cases tenderness was elicited over the lumbosacral joint and was felt to arise from pathological changes in this joint. Possibly in some of these cases the tenderness resulted from a lesion of the fourth and fifth lumbar interspace. In 50 cases no tenderness could be elicited on physical examination, or it was of such little significance that it was not noted. In 39 cases there was tenderness over the region of the sacro-iliac joint on the affected side, which was probably of little clinical significance. In 80 cases, or 80 per cent, there was very definite limitation of motion, particularly in that of flexion of the spinal column.

In 93 of 98 cases in which fluoroscopic examination with radiopaque oil was employed, there was a positive defect; in 4 the procedure was a failure, and in 1 the result was negative. In the last a disc was found at the interspace between the fourth and fifth lumbar vertebræ at operation. In the 2 remaining cases of the series a direct exploration was carried out without a roentgenological examination. Forty-one of the posterior protrusions occurred at the fourth and fifth lumbar interspace, 46 at the lumbosacral joint, 8 at the third and fourth lumbar interspace, 1 at the second and third lumbar interspace, and 4 patients showed multiple protrusions. In this group there were 28 midline or bilateral protrusions of the discs. The remaining 72 cases presented unilateral protrusions.

It is the author's impression after completing this study that a possible explanation of the intermittency of the symptoms is that in some manner a change in position of the dislodged nucleus beneath the annulus fibrosus results in a reduction to somewhat of a normal anatomical position. From the cases observed at the time of operation, one would anticipate that this could occur by a reduction of a protruded nucleus pulposus between the intervertebral bodies, which would permit a collapse of the annulus and a release of the nerve compression. The author also mentions a test which is believed to be of significance in the examination of patients with posterior protrusion, that of a sudden unexpected hyperextension at the lower lumbar vertebræ. When positive, pain is reproduced over the course of the affected sciatic nerve. The mechanism whereby this occurs is probably a narrowing of the posterior interspace with a sudden relative increase in the posterior bulge and sudden pressure on the nerve root.

The treatment of this lesion is confined to the neurosurgical division of the Clinic and consists of laminectomy and removal of the ligamentum flavum and disc, in which procedure the articular facets are preserved. There are many cases which require the consideration and measures of the orthopedist in association with the neurosurgical procedure, and it is essential to have close harmony between the orthopedist and the neurosurgeon in the handling of these cases. The cases in which a combined procedure is employed, that of hemi-laminectomy and removal of the disc and bone graft, include such conditions as spondylolisthesis, separated neural arch without slipping of the vertebral body, and marked narrowing of the intervertebral space with hypertrophic arthritic changes.

**Stookey, B.: Compression of the Spinal Cord and Nerve Roots by Herniation of the Nucleus Pulposus in the Cervical Region.** *Arch. Surg.*, 1940, 40: 417.

While true chondromas of the cervical spine do occur, they are much less common lesions than ruptured intervertebral discs, and it is probable that many lesions formerly called chondromas were actually protrusions of the nucleus pulposus through the annulus fibrosus.

Such cervical protrusions are primarily degenerative lesions, developing slowly, and are not the result of one sudden, severe trauma. Since protrusions of the cervical spine affect primarily the cord and not the roots, the symptoms would be those of a sudden onset if the lesion were due to a sudden trauma and would give unmistakable sudden clinical signs of cord injury, all of which is not true in the usual history of the slow progression of symptoms in a protruded disc.

The symptoms of herniation of a cervical intervertebral disc are due to the direct pressure of the mass on the cord and the roots, and symptoms will vary with the exact position and bulk of the mass. There may be present the syndrome of *bilateral pressure*, depending again on the size and position of the herniation: (1) if the mass is small and medially placed on the ventral surface of the vertebral canal, pressure is exerted bilaterally on the ventral horns and roots, and gives rise to bilateral signs referable only to the ventral gray columns, but (2) if the medially placed mass is large, the signs are indistinguishable from those of a ventral cord tumor. The second syndrome, that of *unilateral ventral pressure*, due to pressure of an off-center mass upon the ventral horn and ventrolateral columns of one side, consists of focal atrophy and crossed dissociated sensory changes. The third syndrome, that of *unilateral root pressure*, is characterized by a unilateral focal muscular atrophy and focal pain, without, of course, any symptoms of pressure on the long fiber tracts.

Vertebral tenderness is seldom of any localizing value. Manometric tests and total protein studies upon the cerebrospinal fluid may add but little in-

formation, since at best no more than a partial block is usually caused by a protruded disc. Air and oil myelography are inconclusive, inadequate, or actually dangerous. X-ray evidence of a narrowed intervertebral disc may be present even in the absence of a herniation, but with any evidence which such tests furnish, together with the localizing clinical signs, a laminectomy is always indicated because it offers the only means of help to these patients. A hemilaminectomy with sufficient bone removal laterally is advised. The dura is opened, if necessary, to avoid undue rotation of the cord, but it is well to perform the enucleation extradurally if it can be accomplished with any degree of ease and accuracy.

JOHN MARTIN, M.D.

**Spurling, R. G., and Grantham, E. G.: Neurological Picture of Herniations of the Nucleus Pulposus in the Lower Part of the Lumbar Region.** *Arch. Surg.*, 1940, 40: 375.

This communication is based on 125 consecutive laminectomies performed for intractable pain low in the back, and sciatic pain. There were 92 cases of frank rupture of the annulus fibrosus with herniation of the nucleus pulposus. The lesion occurred at the fifth lumbar interspace in 51 patients, at the fourth in 39 patients, at the third in 1 patient, and at both the fourth and fifth in 1. In this series the incidence of ruptured intervertebral disc at the fourth and fifth lumbar interspaces was 99 per cent. The diagnosis could be made on the basis of the history and clinical findings alone, without the use of contrast myelography in about 50 per cent of the cases.

The initial symptom of disease of an intervertebral disc is, almost without exception, pain low in the back (lumbago). The onset of the pain is sudden and usually follows trauma, lifting in a bent-forward position, or sudden torsion of the trunk. Shortly after, sciatic pain may occur. Occasionally sciatic pain occurs after a number of attacks of "lumbago." As the pain in the leg increases in intensity, the pain in the back usually diminishes or disappears entirely. During the acute stages the pain, both in the back and in the leg, is intensified by coughing, straining, or sneezing. Paresthesias in the involved dermatotomes commonly accompany the pain in the legs. The paresthesias are not constant, and usually are brought out by certain postures, or by coughing, straining, or sneezing. Observant patients frequently describe a sensory loss which is limited to the involved dermatotomes. Weakness is not a common feature. In some instances, however, weakness limited to one group of muscles is present.

The clinical localizing signs are tabulated by the authors as follows:

*Third lumbar interspace.*

1. Disability of the lower part of the back, with local tenderness at the third lumbar spine and reduction of the lumbar lordosis.
2. Positive Lasègue sign.
3. Positive Naffziger test (pressure is applied over both jugulars until there is a sense of fullness in the head or until the patient's face is flushed, and when the test is positive there is pain or paresthesia in the back of the leg). This is considered by the authors as pathognomonic of intraspinal disease.
4. Reduction or absence of the knee jerk; the ankle jerk is unchanged.
5. Hypesthesia and paresthesias in the fourth and fifth lumbar dermatotomes.

*Fourth lumbar interspace.*

1. Disability of the lower part of the back with stiffness of the lumbar portion of the spine and localized tenderness at the level of the fourth lamina, with reduction of the lumbar lordosis.
2. Positive Lasègue sign.
3. Positive Naffziger test, with paresthesias involving the fifth lumbar, the first sacral, and perhaps the second sacral dermatotomes.
4. Ankle and knee jerks uninvolved.
5. Hypesthesia and paresthesias in the fifth lumbar and first sacral dermatotomes.

*Fifth lumbar interspace.*

1. Disability of the lower part of the back with absence of lumbar lordosis and localized tenderness to pressure over the fifth lumbar vertebra.
2. Positive Lasègue sign.
3. Positive Naffziger test producing paresthesias radiating into the first and second sacral dermatotomes.
4. Diminution or absence of the ankle jerk.
5. Hypesthesia involving the first and second sacral dermatotomes.

DAVID J. IMPASTATO, M.D.

## PERIPHERAL NERVES

**Dumas, R.: Injuries of the Nerves: Late Results of Surgical Treatment and Indications for Operation** (Blessures des nerfs: résultats éloignés du traitement chirurgical et indications opératoires). *Presse méd.*, Par., 1940, 48: 99.

Dumas leaves one with the impression that he is still pessimistic over the results, by and large, of peripheral nerve surgery; to him, at least, the results of such surgery so far have fallen short of the desired and expected goal. His article is a brief but instructive review of pertinent opinions (principally French) since 1883, and he has contrasted the views of a long list of surgeons on the relative merits of early and late suture; on grafts, such as alcohol-fixed grafts, rabbit cords, heterografts of fresh nerves, and fresh autografts; and on indications for operation.

He brings up the matter of the wide divergence of results of peripheral nerve suture in several large series of cases seen during the World War, and he is, like many another surgeon, puzzled by the lack of uniformity in results obtained by the same manner of treatment. He emphasizes the fact that "we should all talk the same language" in evaluating the results of peripheral-nerve repair. The restoration of a nerve is always null, partial, or total; there is no in-between or variation of these conditions.

Several general principles have become reliable guides in peripheral-nerve surgery:

1. In recent injuries, repair of the nerve should be done as soon as possible, after a neurological examination has been made and recorded, and the nerve should be sutured in the approved manner with silk.

2. In old injuries, a *careful* neurolysis is of prime importance; the nerve ends must be fresh and show normal tissue when they are approximated end-to-end; no tension must be allowed on the suture line; no secondary repair can ever be done in the presence of the least infection; the newly sutured nerve should be placed in a fresh, scarless bed of muscle or fat; and only *fresh autografts* are to be used when a graft is found to be necessary. In incomplete lesions, as in the case of lateral neuromas and local indurations without neuromas, one should determine the amount of remaining function as accurately as possible, and by observation over a period of time judge whether or not surgery will offer more than hopeful patience.

JOHN MARTIN, M.D.

**Pozzan, A.: A New Technical Modification in the Method of Laterolateral Anastomosis of the Peripheral Nerves** (Su di una nuova modificazione di tecnica al metodo dell' anastomosi latero-laterale dei nervi periferici). *Arch. ital. di chir.*, 1939, 57: 363.

The superiority of laterolateral anastomosis of the peripheral nerves over the other methods is probably due to the greater limitation of the damage inflicted on the healthy nerve and to the resulting slighter connective-tissue reaction at the anastomotic level; besides, the healthy fibers which may have persisted in the damaged nerve are not interrupted and the remaining partial function of the nerve will not be jeopardized in case of operative failure. The experiments of Pozzan showed that, in successful laterolateral anastomosis of the completely paralyzed peroneal nerve with the tibial nerve, it was sufficient to remove at the point of contact between the two nerves the perineurium of the peroneal and one-fifth of the fibers of the tibial for a distance of 1.5 cm. Unfortunately, anatomical relations are not always as favorable as in the case of these two nerves and some effective means has to be found to bridge the space separating the donor from the receiving nerve. Therefore, the author decided to use autoplastic and heteroplastic transplants of peripheral-nerve tissue, which he anastomosed laterolaterally to the two nerves.

For his experiments, he selected puppies aged not more than two months, because the younger the animal the more rapid and complete is the regeneration of the nerve. Under ether anesthesia, the dogs were prepared for the anastomosis by section of the peroneal nerve close to its origin from the sciatic nerve, and by suture of the two stumps separately to the subcutaneous cellular tissue at a sufficient distance one from the other to prevent any possibility of even indirect connection between them. Then a portion 1 cm. long and involving the perineurium and one-fifth of the fibers was cut out of the lateral aspect of the tibial nerve close to its origin from the sciatic nerve, while an equal portion of the perineurium only was removed from the distal part of the peroneal nerve about 4 cm. from its original section. In 5 cases, a piece of nerve taken from one of the branches of the brachial plexus of the same animal and, in 3 cases, a piece of calf's nerve fixed in alcohol and then kept for some time in sterile physiological salt solution were used as transplants to be fixed laterolaterally to the excised parts of the tibial and peroneal nerves by means of fine silk sutures.

Functional and anatomicopathological studies of the autoplastic transplants made at various intervals after the operation showed that histological evidence of beginning regeneration was present in the anastomotic bridge and in the peroneal nerve after four months, but that no response of the nerve to galvanic stimulation could yet be demonstrated. After six months, the motility of the muscles innervated by the peroneal nerve was being re-established and the nerve responded to electric stimulation; histologically, the regeneration of the nerve fibers was more advanced. After ten months, the functional tests of the leg gave practically the same results as those of the other leg; histologically, the regeneration of the nerve was advanced far enough to allow the conclusion that the trophism of the muscles would be completely re-established: in fact, the muscles already appeared normal macroscopically and microscopically at that time.

On the other hand, the functional tests and the histological examinations of the heteroplastic transplants did not reveal the slightest sign of regeneration even after ten months.

In the practical application of this method, it will naturally be difficult to obtain the necessary autoplastic material, but the complete lack of results with heteroplastic transplants suggests that the results might be quite different if homoplastic material were used. This question will be the object of further studies.

RICHARD KEMEL, M.D.

## MISCELLANEOUS

**Alberti, A.: Perineal Dystonia of Causalgic Type Due to Stretching of the Pudendal Nerve by Aneurysm of the Homonymous Artery, Treated and Cured by Resection of the Vasculonervous Bundle** (Distonia perineale, a tipo causalgico, per distensione del n. pudendo da aneurisma dell' arteria omonima, curata e guarita con trattamento radicale: resezione del fascio vascolo-nervoso). *Clin. chir.*, 1940, 16: 99.

Alberti reports the case of a woman, aged thirty-nine years, who after her first pregnancy, about eighteen years previously, developed some hemorrhoid nodules accompanied by attacks of pain which had become worse lately. She was very constipated. The attacks, which were rare in the beginning, consisted now of painful spasms occurring several times during the day and night and involving the anterior part of the perineum with irradiations around the vagina, the urethra, and especially the clitoris, where the pain assumed the form of causalgic burning. At

times, inflammatory symptoms appeared in the hemorrhoids. Examination revealed the presence of hemorrhoids around the anterior border of the anus and marked anal and vaginal spasm. When the patient was lying on her right side, she felt pulsations inside the pelvis; digital pressure on the right ischiatic process caused tenderness which spread upward deeply into the pelvis. During general perspiration, the perineum was especially involved and was dripping with sweat; the pilocarpine test caused moderate general perspiration with great increase of the perineal perspiration. Surgical intervention was decided upon to remove the hemorrhoids as high as possible because a nodule had been found to extend rather high along the anterior wall of the anorectal canal. However, at operation, an aneurysm of the internal pudendal artery, 2 cm. long, was found about 1.5 cm. above the medial border of the ischiatic tuberosity; the deformed artery, the nerve, and some veins formed the pudendal bundle; the pudendal nerve divided behind the aneurysm, and its two branches were astride the aneurysmal sac. The various elements of the pudendal bundle presented strong adhesions between themselves and with the aneurysmal sac and the obturator membrane, so that mass excision was found advisable. The results of the operation were excellent, as shown by a follow-up examination eight months later.

This is the first case of aneurysm of the pudendal artery found during life and reported in the literature. However, its significance exceeds its anatomical interest because it was the principal factor in the origination of the perineal dystonia which was thought to be caused by the hemorrhoids. The diagnosis was cleared up only by the operative findings. There is no doubt that at least a probability diagnosis could have been made by thorough rectal exploration, all the more so as sensitivity of the ischiatic tuberosity was demonstrated, which is one of the symptoms of homolateral pudendal nerve involvement. On the other hand, the intense localized perspiration of the perineum, which might be interpreted as being connected with general lability of the neurovegetative system, must have been favored by the peculiar structure and innervation of this region: the pudendal nerve contains not only cerebrospinal fibers but also fibers of a sympathetic nature and function, and the pudendal plexus emits parasympathetic filaments and is connected with the pelvic sympathetic system; under the circumstances, endogenous and exogenous stimulation may give rise to the most variable picture of neurovegetative reaction. The cutaneous expression of the sympathetic involvement through the pudendal nerve acquires decisive significance from the fact that it has not reappeared after excision of the nerve. The inflammatory remnants found under the form of connective-tissue adhesions between the elements of the pudendal bundle and the obturator membrane, and the peculiar position of the pudendal nerve, tightly adherent to the aneurysmal sac, explain the reactive condition of the nerve; the various clinical manifestations depend on the complex composition of the nerve.

RICHARD KEMEL, M.D.

# SURGERY OF THE THORAX

## CHEST WALL AND BREAST

**Heiberg, B., and Heiberg, P.: Some Investigations into the Occurrence of Carcinoma of the Breast, with Special Reference to the Ovarian Function.** *Acta chirurg. Scand.*, 1940, 83: 479.

In this intensive review of the literature on the subject, with pertinent observations on the various clinical and experimental works, Heiberg and Heiberg point out that there is a definite relationship between ovarian function and the development of carcinoma of the breast. They further point out that the actual connection is still unknown.

In an endeavor to throw further light on the existing connection the authors undertook a detailed statistical study of 1,200 cases of mammary carcinoma in Copenhagen, as well as an analysis of statistics from Denmark as a whole. In general, the mortality rate from carcinoma in Denmark is definitely greater in unmarried women than in married women. An analysis of statistics showed that mortality from mammary carcinoma increases with age and, therefore, there is no climax near the beginning of the menopause. It was thought that possibly unmarried women tended to seek medical care at a later date than did married women, which influenced the mortality rates. However, this did not prove to be the case. In order to eliminate possible errors in the census, deaths due to croupous pneumonia and carcinoma of the gastro-intestinal tract in unmarried women and married women were compared. No appreciable differences were found.

The authors found that in nearly two-thirds of their group of cases the menopause had not occurred at the age of fifty. This figure is very high, for on the average in Denmark only 20 per cent of the women menstruate at the age of fifty or more. Considerable significance is attached to this fact.

No connection between previous gynecological or endocrine diseases and the development of carcinoma of the breast could be demonstrated.

The authors urge that further detailed histological investigations to distinguish between various groups of carcinoma of the breast be made. They suggest that the preponderance of the disease in unmarried women might be due to the more frequent development of one particular type of carcinoma, which in turn may be connected with a difference in ovarian function.

LUTHER H. WOLFF, M.D.

## TRACHEA, LUNGS, AND PLEURA

**Reisner, D., and Tchertkoff, I. G.: Cystic Bronchiectasis.** *Am. J. Roentgenol.*, 1940, 43: 327.

The authors report a group of 17 cases of cystic bronchiectasis, or polycystic lung, which they consider a distinct clinical entity, different from chronic bronchiectasis.

The ages of the patients varied from eleven to seventy years; 12 were males and 5 females. As a rule, the respiratory symptoms were mild, consisting of a chronic cough, with scanty sputum and frequent colds. Constitutional symptoms were absent unless complicated by other lesions. Physical examination revealed slight changes from the normal. The most frequent physical signs were the presence of numerous moist medium and coarse râles. Roentgenograms showed a honeycombed appearance of the lung fields produced by a cluster of thin walled, closely packed cavities separated by fine trabeculations, which frequently presented fluid levels. There was an absence of infiltrative lesions or fibrosis in the uncomplicated cases.

The authors believe that this condition is of congenital origin and is due to the arrest of development of the terminal bronchioles and the lung parenchyma.

The condition is of importance and should be differentiated from saccular bronchiectasis and tuberculosis. Unless the patients develop complications they usually go through life only mildly handicapped.

JULIAN A. MOORE, M.D.

## HEART AND PERICARDIUM

**Holman, E.: Hemicardiac Hypertrophy Due to Increased Peripheral Resistance.** *J. Thoracic Surg.*, 1940, 9: 262.

Cardiac enlargement may be due to hypertrophy, to dilatation, or to a combination of both. The factors responsible for the enlargement are not always obvious.

This author has studied the problem with a view to determining accurately the exact rôle of peripheral resistance to cardiac hypertrophy uncomplicated by distention of the cardiac chambers, by means of experiments on newborn or on very young puppies. The heart of the young animal was exposed through a small incision, the pericardium was opened, and a silk ligature was placed around the root of either the pulmonary artery or the aorta and tied so as to encircle the vessel snugly, but not to constrict it even slightly. As the animal and its organs grew in size, the vessel remained constricted to its original size at the site of the ligature and a relative stenosis occurred. A litter mate was kept as the control animal.

In this way cardiac hypertrophy, limited to one-half of the heart, was produced by increasing peripheral resistance alone; it was not accompanied nor preceded by dilatation. This hypertrophy occurred on either side of the heart, depending upon the site of the constriction. It cannot, therefore, in the case of pulmonic stenosis be dependent upon an increased coronary flow such as might be invoked as a cause of the left ventricular response to a constriction beyond the coronary arteries. This hypertrophy

was sufficient to produce conspicuous cardiac enlargement, an enlargement which was quite different from that which followed the establishment of an arteriovenous fistula. The study showed further that cardiac enlargement may be due to two very different factors; in pulmonic and aortic stenosis, the enlargement is due to hypertrophy, limited to one-half of the heart. This hypertrophy is due to the increased peripheral resistance against which the cardiac musculature must work. In the presence of the peripheral fistula, the enlargement is almost entirely due to dilatation with thinning of both ventricular walls. In this instance there is a decrease in peripheral resistance but an increase in the volume or bulk of blood flowing through the heart.

Cardiac enlargement observed clinically or roentgenographically, therefore, may be due either to dilatation or to hypertrophy.

J. DANIEL WILLEMS, M.D.

## ESOPHAGUS AND MEDIASTINUM

**Guimarães, S.: A Contribution on the Surgery of Mega-Esophagus: Considerations on 140 Cases** (Contribuição á cirurgia do megaesôfago: considerações em torno de 140 casos). *Cultura méd.*, 1939, 1: 377.

Guimarães states that at present most authors accept the methods of dilatation as the only ones which offer probabilities of success and security in the treatment of mega-esophagus. Many appliances, made of metal or rubber, have been described for this purpose. The author uses an instrument constructed according to his instructions; it has a dilator made of a tube of fine tissue which is placed between two tubes made of rubber fixed proximally to the rubber shaft of the instrument and distally to the protruding steel wire which runs inside of the instrument, and has a removable olivary extremity. The rubber shaft bears the usual marks corresponding to the classical distances of the diaphragm, cardia, and stomach from the dental arches.

The indications and contraindications for the use of dilating instruments must be given exclusively by esophagoscopy. Previous operation or dilatation with sounds does not constitute a contraindication, but caution is recommended in employing the dilating tube, which should not have a diameter of more than 3.5 cm. Only 2 of all the patients attended by the author were excluded from immediate treatment, because of intense esophagitis. Some of his patients presented fibrous cardias which could not have been passed by the instrument without the help of the olivary wire. Although each case had to be considered individually, a routine method was established which took the following points into consideration: use of the dilating tube distended by air pressure, abstention from manometric control, abstention from roentgen control, introduction of the instrument without wire guide, and dilatation varying between 2 and 4 cm. These rules could be applied in the majority of the cases; in only 1 patient was it necessary to use esophagoscopy to introduce the olivary wire through the cardia and to place the dilator.

Before dilating, it is advisable to make the patient regurgitate the contents of the esophageal sac. The patient is seated with the head slightly bent forward, and no anesthesia is used. The instrument passes into the esophagus when the patient makes a swallowing movement or stops breathing, the head is raised, and the instrument penetrates down to the diaphragmatic narrowing; if it does not pass the sphincter immediately, some slight back and forth movements help to overcome the resistance and a peculiar feeling announces the passage of the instrument into the stomach, into which it is introduced several additional centimeters. The instrument is fixed at the dental arch by an assistant and the tube is distended with air by means of a 100 c.cm. syringe. It is impossible to overdistend the tube because of the presence of the tube made of tissue which limits dilatation. The dilatation usually lasts about five minutes. On the day of the intervention, the patient is kept in bed and given a liquid diet; on the following day, he is allowed to get up, and takes a liquid and soft diet; after that, the diet is unrestricted. The results have been excellent: 140 patients have been treated. Two patients have died from mediastinitis caused by rupture of the esophagus: these accidents occurred among the first patients treated, because of excessive dilatation with tubes having a diameter of 4.5 and 5.5 cm.; since then, none of more than 4 cm. have been used. No patient has been dilated more than 6 times. In 26 cases there were recurrences necessitating another series of treatments: in 11, the recurrence appeared during the first six days after the end of the treatment, and in 15 between eight days and seven months after the treatment.

RICHARD KEMEL, M.D.

**Noehren, A. H.: Artificial Skin-Lined Antethoracic Esophagus for Impermeable Stricture.** *Surgery*, 1940, 7: 364.

The making of an extrathoracic esophagus has a very limited field; namely, (a) in cases of benign stricture that are absolutely impermeable by all known methods, and (b) in cases of malignant stricture in which the cancer has been successfully removed.

When indicated, the making of an esophagostomy and the introduction of a skin tube down the front of the chest is the simplest and safest method. The only disadvantage is the difficulty or impossibility of making a connection between the lower end and the gastric fistula, but this gap can be easily bridged by a shorter rubber tube.

The author reports the case of a young woman twenty-four years of age in whom an artificial extrathoracic esophagus was constructed for a benign stricture secondary to a burn by a caustic fluid. The procedure was carried out in several stages. The operation is described in detail and is well illustrated.

SAMUEL H. KLEIN, M.D.

**Bernou, A., Fruchaud, H., and Marecaux, L.: Thoracoplasty and Excessive Mobility of the Mediastinum** (Thoracoplasties et flottement médiastinal). *Arch. méd.-chir. de l'appar. respir.*, 1930, 14: 34.

Bernou and his associates note that excessive mobility or "floating" of the mediastinum is a serious complication of thoracoplasty. With improvement in the technique of thoracoplasty, it occurs less frequently, especially if an extensive one-stage operation is avoided. Since 1934, the authors have adopted the practice of resecting the lower ribs at the first stage of thoracoplasty and never resecting the first rib until the second stage. Excessive mobility of the mediastinum was noted in a few cases even with this method, although no deaths resulted; thus, the authors made a special study of the mobility of the mediastinum prior to operation. For this purpose a fluoroscopic examination was made with the patient in lateral decubitus, lying first on the left side with a vertical screen at the back, then on the right side with the screen in the same position; the rays were centered perpendicularly to the screen. The distances of the "point" of the heart to the axillary line were recorded in each position; the difference between the two measurements at times was only from 1 to 1.5 cm., which indicated no excessive mobility of the mediastinum; if the difference was over 3 cm., the mediastinum was excessively mobile. Even differences of from 2 to 3 cm. should be considered in deciding on the technique of operation.

If the fluoroscopic examination by this technique shows a displacement of from 4 to 6 cm., the anterolateral subpectoral route is never employed for the thoracoplasty, the paravertebral or subscapular route is the method of choice. In such cases the extent of the rib resection on the second, third, fourth, and fifth ribs in the first stage of the thoracoplasty is limited. The second stage is delayed at least three, and sometimes four, weeks; at this second stage the first rib may be entirely resected and the resection of the other ribs may be extended. A small portion of the sixth rib may be resected, but this should not be done if the displacement of the mediastinum is found to be from 5 to 6 cm. in the pre-operative examination. In resection of the ribs by the subscapular route, the transverse processes of the vertebræ are left intact. With this technique no complication from excessive mobility of the mediastinum has been observed, and the operation causes much less shock to the patient. ALICE M. MEYERS.

## MISCELLANEOUS

**Ransom, F. T.: Notes on Gunshot Wounds of the Chest.** *J. Thoracic Surg.*, 1940, 9: 278.

The author writes about his experiences in China, and his article is probably one of the first accounts, if not the first, of gunshot wounds in the chest in the present war in China.

He begins by reviewing the history of gunshot wounds in the fifteenth century. He then gives the figures for some past wars, dealing with the number of chest wounds and the number of deaths among the wounded with chest wounds. He states that about 1 wound of every 12 is of the chest. The number of men who die on the field of chest wounds is from one-third to one-half of the total number who are killed, but the more important figures are those which deal with the deaths among the wounded who are taken off the field to the hospitals. These figures are very enlightening. They show that the English in the war of the Crimea lost 79.2 per cent of all men who were wounded in the chest and who arrived at the hospitals for treatment. The figures then show a definite progress and trend through the American Civil War, the Franco-Prussian War, the Spanish-American War, the Boer War, the World War, and the Sino-Japanese War of 1937. In the last war the wounded who died from chest wounds after being treated in the hospital amounted to 14.8 per cent. These figures definitely show the tremendous strides which have been made in the treatment of chest wounds.

The author then relates his own studies of 150 cases of chest wounds during the hostilities which took place in the vicinity of Shanghai, China, in 1937.

Pneumothorax is a most important consideration in the treatment of chest wounds. Mediastinal flutter is of great significance because of its effect upon the great veins which carry blood to the heart. The systolic output is dependent upon the diastolic inflow, and the mediastinal flutter causes periodic obstruction to both the superior and inferior venæ cavæ. The symptoms of open pneumothorax are due, therefore, to a circulatory disturbance rather than to the respiratory disturbance *per se*.

Other important points are the rapid loss of heat from the chest and the great tendency toward infection. The size of the opening in the chest wall which is compatible with life is of importance also, and bears a direct relationship to the vital capacity of the patient. Tension pneumothorax produces even more marked symptoms of distress than the open variety because the pressure in the pleural cavity of both sides approaches a positive value. When the condition is present on the right side, ill effects are produced more rapidly than when it is on the left side, for the right heart and great veins are more sensitive to pressure than the left heart and the main arterial trunks. A tension pneumothorax, unless relieved, invariably leads to a fatal outcome.

Blood in the pleural cavity will cause collapse of the lung to a degree dependent upon the amount of fluid involved. There is a tendency toward spontaneous arrest of bleeding from the lung when a balance is obtained between the collapse of the lung and the pressure in the pleural cavity. Removal of large quantities of blood from the chest cavity is frequently found to cause unpleasant and dangerous cardiac respiratory symptoms which can be counteracted by air replacement.

Cardiac tamponade, when more than 200 c.cm., exerts definite pressure upon the heart. The thicker-walled ventricles are not adversely affected but the

auricles and the great veins are found to be definitely affected.

Practically all of the cases of the author consisted of wounds of the penetrating variety. Some of these varied from small, almost immediately sealed bullet holes, to large and gaping openings in the chest wall. Thoraco-abdominal wounds were very few, and most of these led to death before the patient reached the hospital. Wounds of the through-and-through variety were very numerous and the exit wound was sometimes larger than the entrance wound, sometimes the same size, and sometimes even smaller. A certain number of soldiers had retained projectiles in the chest. In some, the projectile had stopped in the spine or had gone into the abdomen.

Shock and collapse were present in a marked degree in nearly all cases. Pneumothorax was also present in nearly all cases. In 2 cases tension pneumothorax was observed. Hemothorax was almost invariably present. Pyothorax was a common sequel, and frequently all three, pneumothorax, hemothorax, and pyothorax, were combined. Emphysema of varying degree was also seen. One man had emphysema which resulted in the closure of both his eyes, and his scrotum became the size of a football. He was described as having the appearance of a gigantic frog. Brachial-plexus injuries were found in 2 soldiers and an axillary aneurysm was found in 1. Among the remote complications were septicemia, pyemia, and cerebral abscess; such complications as dysentery, malnutrition, and beriberi were also the cause of several deaths.

The examination of patients was necessarily always done during rush periods. When first admitted, examination was often perfunctory. A notation was made of the site and size of the entrance wound, the site and size of the exit wound, and whether or not the wound was of the "sucking" variety. If the last was found instructions were issued that the wound must be covered at once by a large wet dressing. Great stress was placed on the degree of shock present and the amount of external hemorrhage. The position of the apex beat, the position of the trachea, and the presence of dullness were likewise recorded. Effusions, if present, were examined by the naked eye or the microscope, and sometimes cultures were made. Fluoroscopy and x-ray pictures were used extensively.

All patients were examined once a week by means of the fluoroscope. In the cases of empyema, a chart was kept showing the size of the cavity from day to day. All patients with cavities were likewise examined with the thoracoscope but nothing striking was discovered.

Treatment consisted first of attending the shock and bleeding. This was done by the administration of morphine and the application of heat. Blood transfusions could not be given because there were no typed donors available; intravenous saline solution was used instead. A good many patients with through-and-through bullet wounds made a rapid recovery after a simple antiseptic dressing and the administration of morphine and rest. After the patient recovered from the initial shock, the usual practice was to excise the wound, remove portions of the fractured ribs, arrest the hemorrhage in the parietal wound, remove foreign bodies if easily accessible, and, if possible, close the wound by suture. No extensive search for foreign bodies was carried out and no attempt was made to arrest hemorrhage from the lung itself. The first principle of treatment was to close the wound in the chest wall; the hemothorax was treated later.

Anesthesia for most of these operations was local, but sometimes this was supplemented with ether or evipan.

Open pneumothorax was treated with saline infusion for the shock, and an early production of a closed pneumothorax by suture or by packing. Tension pneumothorax was treated simply by letting out the air. Hemothorax was dealt with by controlling the hemorrhage from the chest wall and by closing the wound. It was believed that if the wound involved a large vessel at the root of the lung, death was certain to occur anyway, but if the wound involved only peripheral vessels these would be controlled by the pressure of the hemothorax and the pneumothorax. Aspiration was not done for several days unless signs of pressure or infection appeared early, but after a few days the blood was aspirated and replaced with air. However, never more than 1,000 c.cm. were aspirated at a time. Pyothorax was a very common complication and usually followed hemopneumothorax. The treatment of these cases consisted, as far as possible, of drainage with avoidance of an open pneumothorax during the early stages of the empyema. Early sterilization with obliteration of the cavity was attempted and the nutrition of the patient was carefully maintained. Of 35 patients with empyema, all but 3 healed in a period of four months.

Retained projectiles in the chest did not as a rule give rise to troublesome symptoms. In a few cases presenting such symptoms, these bullets or shell fragments were removed.

The total number of admissions to the hospital in this period of the war consisted of 1,186. Of these, 115 were patients with chest wounds, and 17 of these died from these wounds. Therefore, 10 per cent of all the wounded had chest wounds; and 14.8 per cent of these who reached the hospital died.

J. DANIEL WILLEMS, M.D.

**Marcotte, R. J., Phillips, F. J., Adams, W. E., and Livingstone, H.: Differential Intrabronchial Pressures and Mediastinal Emphysema.** *J. Thoracic Surg.*, 1940, 9: 346.

Tuffier of Paris in 1896 passed a metal tube through the larynx and anesthetized a patient in this manner, following which a partial lung resection was performed. This is the first case in which an intratracheal insufflation was done. The authors give a rather complete historical background for the method. A series of clinical cases along with a few com-

plications, and also some experimental evidence of complications are given with the following conclusions:

Intratracheal or positive-pressure anesthesia may result in serious or fatal complications. Increased intrabronchial pressure either by intratracheal or mask-anesthesia technique may produce deleterious effects by overdistention and laceration of the intrapulmonary tissue with subsequent development of mediastinal emphysema and pneumothorax. Intrabronchial pressure depends chiefly upon the patency of the outlet, rather than upon the pressure at which the gases are forced into the lungs. Intrabronchial pressure of 18 mm. of mercury or below seldom, if ever, causes mediastinal emphysema in dogs. Extremely high intrabronchial pressures are necessary to cause emphysema about the neck and face or to cause right cardiac failure in dogs. Pneumothorax may easily occur following mediastinal emphysema. Once emphysema has developed, it may be increased at a pressure lower than that necessary to initiate it. PAUL MERRELL, M.D.

**Adams, W. E.: Differential Pressures and Reduced Lung Function in Intrathoracic Operations.** *J. Thoracic Surg.*, 1940, 9: 254.

Before undertaking intrathoracic operations, it is important to know: (a) the vital capacity preceding operation, (b) the functional capacity of the heart, and (c) the oxygen-carrying capacity of the blood. It is also important to know the amount of functioning lung during operation, and how to maintain it during and after operation.

These various factors depend upon:

1. The expected diminution of lung function due to removal of or collapse of lung tissue.
2. The amount of blood loss during operation.
3. The amount of diminished respiratory effort.
4. The effect of the operation upon the cardiac output.

The author states that the vital capacity necessary to sustain life in healthy animals is less than 50 per cent and may be less than 25 per cent. Animals can stand a gradual reduction of vital capacity much better than a sudden reduction. In view of this, when clinical conditions require the removal of lung tissue involving both sides of the chest, it should be much safer to remove the tissue in two or more operations from three to six months apart.

The maintenance of sufficient lung function during a surgical pneumothorax is of paramount importance to the success of the operation. Positive-pressure intratracheal anesthesia permits this. However, this type of anesthesia is attended by certain hazards and disadvantages. Mediastinal emphysema and pneumothorax may occur; these result from tears of the alveolar walls, the air travelling along the vessels in the interstitial tissue to the root of the lung into the mediastinum, and the pneumothorax is secondary to the emphysema.

In experiments on dogs an increasing drop in the blood pressure with increasing intrabronchial pressures was demonstrated. Routinely intrabronchial pressures of 24 mm. of mercury were accompanied by the development of mediastinal emphysema in dogs. In cats the necessary pressure was 20 mm. mercury.

Cases of mediastinal emphysema in human beings during intratracheal anesthesia have been reported.

It takes intratracheal pressures of from 52 to 58 mm. of mercury to produce a rupture of the visceral pleura, but Adams reports a mediastinal emphysema following a pressure of only 11 mm. mercury in 1 patient.

Because of these dangers Adams uses simple pressure face-mask anesthesia for most cases and reserves intratracheal anesthesia for the cases with large quantities of purulent sputum, in which it is necessary to maintain an adequate airway and aspirate secretions.

He cautions against the use of high pressures and states that lung re-expansion should be brought about by aspiration of air from the pleural cavity rather than by increase of the pressure of the anesthetic gas. JULIAN A. MOORE, M.D.

# SURGERY OF THE ABDOMEN

## ABDOMINAL WALL AND PERITONEUM

**Massone, A.: Congenital Superficial Inguinal Hernia** (Sull'ernia inguino-superficiale congenita). *Clin. chir.*, 1939, 15: 975.

From the common inguinal hernia, the superficial inguinal hernia is distinguished essentially by the subcutaneous site of the sac which, instead of descending in the scrotum, is interposed between the superficial and aponeurotic fascia. Kuester, who first described this variety of hernia, did not recognize its congenital nature nor its constant association with anomalies of the testicle and with shortening of the spermatic cord. Consiglio, who recently published an important paper on this subject, believed that this hernia is probably caused by an attitude of hyperextension and hyperadduction of the thighs in utero, associated with an oligopolyhydramnios. Such an attitude would be an obstacle to the formation of the scrotum and to the descent of the processus vaginalis, and the latter might follow the route of least resistance, between the superficial fascia and the aponeurosis.

Fourteen cases are presented and the following conclusions are drawn: (1) the Kuester hernia is a rare variety of congenital inguinal hernia which usually becomes apparent after childhood; (2) there were no anomalies in the insertion of the gubernaculum testis in these cases; (3) there was no history suggestive of an oligopolyhydramnios nor of any other cause for fetal hyperextension and hyperadduction; and (4) the theory of Consiglio appears the most logical of those that have been offered.

FRANK MCDOWELL, M.D.

## GASTRO-INTESTINAL TRACT

**Jennings, D.: Perforated Peptic Ulcer: Changes in Age Incidence and Sex Distribution in the Last One Hundred and Fifty Years.** *Lancet*, 1940, 238: 395, 444.

All the readily available papers on acute perforation plus "a mass of unpublished material in England and abroad" have been studied by the essayist. He concluded that it is possible for the first time to summarize evidence which leads to the conclusion "that distinct groups of ulcer cases exist. Their incidence varies independently; *and that the present common type of pyloric ulcer was relatively uncommon up to recently and that its increase is a true increase and not merely the result of better diagnosis and hospital services.*" These original conclusions are based upon the assumption that the clinicians early in the 19th Century not only could make an accurate diagnosis of perforated ulcer, but that enough patients with this condition came to them, and they published enough reports to permit statistical evaluation.

The essayist thus goes back to Gerard, who was Professor of Medicine in Paris in 1803, and also quotes material collected from Swedish, German, and English clinics and including Bogan's report in 1937. All of this material from Northwestern Europe leads to the same conclusions. In the early part of the 19th Century and up to approximately 1900, 3 of every 6 free perforations into the peritoneal cavity occurred in young women less than twenty-five years of age, 1 occurred in an elderly woman, 1 in an elderly man, and 1 in a young man. Since 1920, 1 of every 10 perforations has occurred in elderly women and 9 have occurred mostly in middle aged or young men. The perforations which formerly occurred in young women, and formed a sharply defined group, increased rapidly at the beginning of the 19th Century and disappeared completely and suddenly at the beginning of the 20th Century. According to the essayist this type of ulcer must therefore have been due to something in the environment or mode of life.

In addition, perforated pyloric ulcers in men can also be shown statistically to fall into at least two independent groups. One group is closely associated and is inseparable from perforations of the lesser curvature. It has a similar incidence to that of perforation in women since 1920. The other group tends to affect younger men and has recently undergone a large increase throughout Northwestern Europe and the English speaking countries. This increase has been estimated to be from 300 to 600 per cent.

The author promises to discuss the possible environmental factors responsible for the 3 main types of perforation at a later date, and finally urges that perforated peptic ulcers and many other so-called constitutional diseases be reported to the health authorities because such statistics would demonstrate transition periods which probably would be of great service in elucidating the causative mechanism and instigate a campaign of prevention.

SAMUEL J. FOGELSON, M.D.

**De Fine Licht, E.: The Roentgen Diagnosis of Ileus** *Acta radiol.*, 1940, 21: 32.

During a period of four years there were 142 patients with roentgenological findings resembling ileus at the Gentofte County Hospital, Denmark. There were 50 who were treated with prostigmin. In 33, verified obstruction of the small intestine was present, and in 25 others obstruction of the large bowel was found. There were 22 patients with paralytic ileus, and in 12 evidence of ileus from a variety of causes, such as mesenteric thrombosis, tumor of the pancreas, and trauma to the abdomen, was present. These patients were treated according to their clinical findings.

It was found that the roentgen diagnosis of ileus, when based on the finding of fluid levels, is on the whole of considerable diagnostic value. The mere accumulation of gas in the small intestine does not justify a diagnosis of ileus. For prognosis and as an indication for operation, the single roentgen examination is of no particular value. It becomes valuable, however, if the examination is repeated, since it is then possible to observe any changes in the degree or extent of the ileus. Whether an ileus is paralytic or mechanical cannot be determined with certainty by roentgen examination except that an opaque enema will not infrequently decide this in the large bowel.

Roentgenological pictures similar to those in ileus are often found after an operation and in cases of abdominal trauma. The absence of fluid levels is rare in ileus and if both fluid levels and abnormal gas accumulation are absent, the probability of existing ileus is slight. MANUEL E. LICHTENSTEIN, M.D.

**Tosonotti, T.: Primary Simple Ulcer of the Small Intestine** (L'ulcera semplice primitiva del tenue). *Policlin.*, Rome, 1940, 47: sez. chir. 30.

Tosonotti adds 1 case of simple primary ulcer of the small bowel to the 75 already reported in the literature. These were found for the most part in the ileum and were classified as acute or chronic. The former type was described for the first time in 1833 by Leotta as a cleanly demarcated area of necrosis in which signs of inflammation were absent or minimal, consisting at most of a slight margin of infiltration. The chronic type, on the other hand, was characterized by extensive induration involving the margins and base of the lesion, as well as contiguous portions of the bowel wall, and frequently causing adhesions with approximated loops of gut.

The jejunal ulcer presents a syndrome which is predominantly dyspeptic; it is characterized by anorexia, acid eructations, occasional vomiting, and pain which usually comes on some time after eating and may be burning or cramp-like; this pain is referred to the epigastrium and left upper quadrant; it is brought out by deep palpation and alleviated by alkalis. Hematemesis and melena may be present. These features, with negative roentgen examination of the stomach and duodenum, should direct suspicion toward the jejunum.

In the ileum, on the other hand, the simple ulcer is manifested by sudden crises of colic localizing in the lower abdomen in the left or right quadrant, diarrhea, and possible melena. Here, too, the pain is periodic and interspersed with periods of remission. It is plain that in the latter case differentiation will be difficult from perforations of an acute appendix or a Meckel's diverticulum. The etiology and pathogenesis of this lesion, as of the peptic ulcer, are controversial. The author believes that the cause is primarily vascular, and as basis for his conviction points out that the small vessels which supply the intestine are essentially end-arteries and their occlusion would result in infarct formation. Further, the round form, somewhat coned out, with clean margins as if punched out in normal mucosa, and the sudden onset without a history of intestinal disturbances offer further evidence of a vascular etiology. It is further hypothesized that toxins such as alcohol and nicotine, which are excreted through the gastrointestinal tract, may play a secondary rôle in the development of such ulcers. The interesting suggestion has been made in this connection, as in the case of ulcers occurring in Meckel's diverticula, that they are due to ectopic islands of gastric mucosa. There are many reports, however, in which histological examination has failed to reveal such evidence. The treatment for this entity is strictly surgical, because of the marked tendency toward ulceration which characterizes the lesion. EDITH FARNSWORTH, M.D.

**Westermann, J. J., Jr.: The Rôle of Surgery in the Management of Duodenal Ulcer.** *Ann. Surg.*, 1940, 111: 338.

A surgical procedure for any pathological condition must fulfill the following requirements if it is to be successful: satisfactory immediate recovery, brief uncomplicated convalescence, early return to usefulness, and permanency of cure. Sixty-four consecutive cases of chronic duodenal ulcer treated by gastro-enterostomy were studied to determine to what degree this procedure fulfilled these stipulations.

The objections of the majority of surgeons at the present time to posterior gastro-enterostomy in the treatment of chronic duodenal ulcer is based almost entirely upon the fact that it is so frequently followed by jejunal ulcer. The literature favoring gastric resection, however, shows no distinction between partial gastric resection and subtotal gastric resection. That partial resection is frequently followed by jejunal ulcer is already recognized, and subtotal resection is not immune to this complication. However, while subtotal gastrectomy is a satisfactory operation and fulfills the last requirement, its immediate mortality and postoperative complications will never be eliminated. The author cannot agree with the surgical teaching which recommends subtotal gastrectomy as the only procedure for cure of chronic duodenal ulcer. In the hands of those with less experience smaller portions of the stomach will be resected and the mortality and immediate complications will be high without insurance of permanent cure.

Gastro-enterostomy is not a haphazard fistula between some part of the posterior gastric wall and the jejunum, but a definite well planned, carefully placed opening between a certain limited area of the stomach wall and a corresponding segment of the jejunum. A few of the important features are: (1) the stomach site falls along a line from the lesser to greater curvature drawn obliquely downward from left to right; (2) the lower angle of the stoma falls below a line bisecting the body of the stomach; (3) the serosa of the jejunum is buttressed to serosa of the stomach for an inch above the upper angle of

the stoma; (4) the opening in the lesser sac is affixed to the stomach wall above the stoma; (5) the jejunal site is arbitrarily taken to allow the jejunum to fall naturally without angulation when the stomach is replaced; and (6) the size of the opening will vary with the size of the stomach, but will not be less than 1½ in. in diameter. No clamps and no non-absorbable sutures are used. All bleeding points in the stomach and jejunal walls are tied. Two sutures are used, one continuous for the serosa, and one of a self-inverting type for the mucosa. It is important not to place the stoma near the pylorus.

In the author's series of 64 consecutive cases there were 2 postoperative deaths (3.12 per cent). One followed wound disruption and a pulmonary complication following resuture of the wound. The second was secondary to obstruction of the distal jejunal loop from dense adhesions. The results were unsatisfactory in 5 patients (7.6 per cent). One patient developed a definite jejunal ulcer, which was proved at autopsy. It was possible to follow 54 cases continuously after operation. Thirteen of the patients were followed for ten years or longer; 25, from five to ten years; and 16 from one to five years. From the results obtained in these patients the conclusion is drawn that posterior gastro-enterostomy in the surgical management of duodenal ulcer has met the specified requirements essential to justify continuance of its use. SAMUEL J. FOGELSON, M.D.

**Rossi, V.: Isoperistaltic Supraduodenal Choledochoduodenostomy. Indications, Technique, and Late Results** (La coledoco-duodenostomia sopraduodenale isoperistaltica. Indicazioni, tecnica e risultati lontani). *Arch. ital. d. mal. dell' appar. digerente*, 1939, 8: 419.

The author briefly reviews the historical development of choledochoduodenostomy. Until 1899, there were only 2 successful cases (those of Kocher and Sprengel). The bad results which may follow the procedure are discussed.

The various indications and contraindications are stated. The most common indications are malignant lesions of the common bile duct, intraluminal obstruction of the common duct, chronic pancreatitis, congenital or cicatrical stenosis of the common duct, spasm of the sphincter of Oddi, and tumors of the papilla of Vater or of the head of the pancreas. Contraindications may be present as in patients in whom the common bile duct and duodenum cannot be exposed sufficiently because of adhesions, in patients who are poor risks or those with serious hepatic insufficiency, and in patients with marked changes in the wall of the duct because of purulent processes.

The technique, as described by the author, consists of exposing the supraduodenal part of the common bile duct by a longitudinal incision and mobilizing the hepatoduodenal ligament (Fig. 1). The wall of the common bile duct is then attached to the duodenum in an isoperistaltic manner by a continuous suture of catgut for a distance of about 3 cm. The common bile duct and the duodenum are

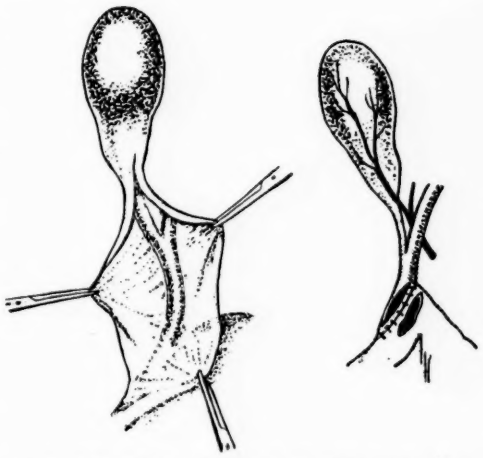


Fig. 1. left. Opening of hepatoduodenal ligament and exposure of the retroduodenal portion of the common bile duct.

Fig. 2. Author's technique of anastomosis of the common bile duct to the duodenum.

incised longitudinally and parallel to the first row of sutures, a stoma which is larger than one made by transverse incisions thus being formed (Fig. 2). Closure of the anastomosis is accomplished in the classical manner with the use of continuous catgut sutures. Cholecystectomy is almost always done as a final stage.

The author states that from July, 1930, to August, 1938, this procedure was performed in 55 cases: 13 (23.6 per cent) males and 42 (76.4 per cent) females. The ages ranged from fourteen to sixty-six years with the largest number in the fourth decade. There were 7 (13.7 per cent) deaths. Of the surviving 48 patients, 23 are in good health, 5 died of intercurrent diseases, 1 died of carcinoma of the pancreas, and 1 of persistent icterus. Of 41 patients, 28 (68.3 per cent) were cured, 6 (14.6 per cent) were benefited, 3 (7.3 per cent) presented fair results, and 4 (9.8 per cent) showed no improvement in their condition.

MICHAEL DEBAKEY, M.D.

**Marshall, S. F.: Regional Ileitis.** *New England J. Med.*, 1940, 222: 375.

Benign, non-specific, granulomatous tumors of the bowel and inflammatory tumors of the bowel were problems of the physician for many years. From the time of Senn's description of inflammatory bowel tumors (1895) up to the present day, the literature contains many instructive reports, all leading more or less to the present study.

The author's paper is based on 48 cases of regional ileitis observed at the Lahey Clinic, Boston, during the last six years. Clinical data and roentgenological findings were the basis of the diagnosis. In twenty-

Fig. 1. Roentgen-ray findings in regional ileitis. The patient was a man, aged twenty-six, with symptoms for over six years. The small bowel is obstructed by a cicatrizing process. Note the marked narrowing ("string sign") of the terminal ileum. The arrow points to a fistulous tract between adherent involved loops of ileum. Operation, a two-stage resection of the ileum and ascending colon, was followed by recovery.

nine patients who were operated upon, the diagnosis was confirmed by pathological examinations of the resected segments of bowel. From Crohn's first description of regional ileitis, it was thought that the lesion was confined to the terminal ileum. Since that time observers have learned that it may be found anywhere in the ileum, jejunum, or colon. It does not always occur in a continuous inflammatory process, as frequently normal segments of bowel may intervene between the diseased portions. Because of this newer observation, the term "regional ileitis" has been replaced by "cicatrizing enteritis," "regional enteritis," "chronic ulcerative enteritis," and "nonspecific granuloma of the intestine." The pathology varies with the stage of the disease. In the acute stage the bowel is thickened and hyperemic; there may be edema of the bowel wall and at the mesentery, and enlarged lymph nodes. In the common chronic process, all layers of the bowel wall are involved; they are characterized by mucosal ulceration and by great thickening of the submucosal and muscular layers. Infiltration of all intestinal coats with mononuclear cells is found especially in the mucosal layer. Giant-cells occur at times and frequently imitate the picture of a tubercle. The bowel lumen is reduced by extreme thickening of the bowel wall and by cicatricial contractions. Ulcerated areas may perforate and result in abscesses and fistulas between adherent loops of bowel, or to the exterior through the abdominal wall. A diagnosis of tuberculosis of the terminal ileum and cecum has frequently been made in this disease, but tubercle bacilli have not been found. The disease is chronic, progresses insidiously, and develops a palpable abdominal mass, with complications as noted. Its cause is not established, but a dysentery bacillus, lymphatic disease of the mesentery, lymphadenitis of early childhood, and other conditions were suggested.

Symptoms of regional ileitis are pain in the right lower quadrant, associated with nausea, diarrhea, loss of weight, and anemia; later, a palpable mass in the abdomen may be felt. The course is that of a chronic progressive inflammatory process persisting for months or even years. The onset is easily interpreted as an acute appendicitis. Many errors can be avoided by carefully examining the ileum when the findings of appendicitis are not definite at operation. Symptoms of intestinal obstruction, though rarely complete, are not uncommon: patients complain of distention with crampy abdominal pain and vomiting. Roentgenological examination often shows constrictions in the lumen of the bowel, with dilated loops proximal to the area of stenosis. The usual complications are internal or external fistulas and perforations into adherent loops of bowel or through the anterior abdominal wall with all the concomitant discomforts.

Roentgenological examination will give positive evidence of the diagnosis (See Fig. 1).

Ileocolostomy versus radical resection has been much discussed. Spontaneous remission of the disease occurs in many cases; this fact appears to support ileocolostomy. However, in advanced cases with marked granulomatous changes, stenosis, obstruction, and ulceration, the only permanent cure is resection of the affected segment of bowel. If the small intestines are greatly involved in many areas, medical treatment must be given as little can be accomplished by surgery and the condition will continue to get worse. Operation in very acute regional ileitis should be avoided. If a laparotomy becomes necessary to establish the diagnosis or to rule out appendicitis, the abdomen should be closed without intra-abdominal surgery, or after a simple ileocolostomy is done. Appendectomies done in the presence of acute regional ileitis often result in external fistula formations. Lahey prefers the Mikulicz resection of the terminal ileum, cecum, and ascending colon in a two-stage operation, as it is by far the safer procedure. Forty-eight patients with regional ileitis were observed during a period of seven years. A two-stage method of resection was the

operation of choice. In 22 patients, resection of the involved loops was done without a fatality. Of 29 patients who were operated upon 2 died.

MATHIAS J. SEIFERT, M.D.

**Beluffi, E. L.: A Case of Perforating Acute Terminal Ileitis Associated with Submucosal Fibromyoma of the Terminal Ileum** (Su un caso di ileite terminale acuta perforativa associata a fibromioma sottomucoso dell'ileo terminale). *Clin. chir.*, 1940, 16: 65.

Beluffi discusses the case of a man, aged thirty-six years, who for three days had suffered from abdominal pain in the region of the umbilicus, accompanied by vomiting and moderate abdominal defense of the right quadrants, when he suddenly developed the typical symptoms of intestinal perforation. The diagnosis of peritonitis due to acute appendicitis was made, but at operation the appendix was found to be normal, while the last portion of the ileum was markedly inflamed and presented several perforations and ulcerations over a tract of 20 cm., beginning just beyond the ileocecal valve. A submucosal fibromyoma, the size of a large nut, was discovered about 8 cm. higher up. Entero-anastomosis was performed and the patient died three hours after the intervention. Necropsy revealed no special lesions of the parenchymatous organs or of the ileum higher up, except for a moderate hyperemia of Peyer's patches. Histological examination of the resected portion showed that the mucosa was greatly thickened and was the seat of a fibrinous purulent hemorrhagic infiltration which reached its greatest intensity in the submucosa and decreased gradually in the other layers. The slightly swollen Peyer's patches did not present any particular histological characteristics. Cultures of the contents of the involved intestinal loop developed an enterococcus; those of the spleen were negative. Widal's test was negative.

The perforations were not due to thrombo-embolic circulatory changes, incarceration, compression anemia, trauma, or worms. Typhoid was excluded by the history, the symptoms, the histological examination, and the negative Widal test. The perforations could not be attributed to "simple or round ulcer of the small intestine." The type of the observed changes left as the only possibility the diagnosis of perforating primary acute terminal ileitis.

Similar acute primary phlegmonous changes in the terminal ileum have been reported by various authors during the past years; they showed the same characteristics as in the present case, but no perforations, and nearly all of the cases came to operation with the diagnosis of acute appendicitis. However, various cases with perforation have also been described, and it must be admitted that the tendency toward perforation is one of the basic characteristics of terminal ileitis, but the slowness with which the perforation occurs allows the necessary time for the involved part to contract adhesions with the neighboring organs. Perforation in acute cases cannot be considered as an exception; it depends more on the rare coincidence of aggravating factors. The site of predilection of the perforations seems to be the mesenteric border.

The cause of the present case is not clear; the bacillus coli and enterococcus were found, but they were not in sufficient numbers to be responsible for the changes. The lesions of the mucosa suggested that they were secondary to a submucosal process. A hematogenous origin cannot be excluded because the patient had had angina with fever shortly before developing the ileitis, and similar cases have been reported. Besides, the ileococeco-appendicular segment is more exposed to infectious attacks than the other parts of the intestine. It did not seem that the presence of the fibromyoma had had any influence on the pathogenesis of the disease.

As spontaneous resolution of acute ileitis appears to be practically the rule, it is permissible to abstain from any intervention; in case of occlusion, operation is indicated, preferably enterostomy. If the lesions are serious and do not regress, resection in one stage followed by ileo-ileostomy or ileocolostomy is the ideal intervention. RICHARD KEMEL, M.D.

**Ravenel, W. J.: Submucous Lipoma of the Large Intestine, with Case Report.** *Radiology*, 1940, 34: 217.

A submucous lipoma of the large intestine is a quite uncommon fatty tumor which arises external to the muscular layer of the gut and protrudes into the lumen of the bowel. It is benign, but is often confused with a carcinoma. Such tumors usually appear singly, but they may be multiple and vary in size from 1 to 12 cm. The average size seems to be 4 cm. in diameter. They may be sessile or pedunculated; and lobulated, rounded, ovoid, or pyriform.

The symptoms are exceedingly variable. There may be bleeding, vague pains in the abdomen, and obstruction. Intussusception is usually responsible for the obstruction because it interferes with peristalsis. Obstruction may be due to the size of the tumor protruding into the lumen, and the tumor may become swollen as a result of interference with the blood supply.

Carcinoma is usually the diagnosis that is made because of the loss of weight, bleeding, and low hemoglobin estimation which usually accompany the tumor. Of these lipomas, 72 per cent are said to occur in the cancer age. Occasionally the tumor can be demonstrated to be polypoid by x-ray examination. The long duration of the symptoms or the finding of a polypoid tumor at x-ray examination may suggest a benign lesion. However, the most common polyp of the colon is the adenoma which may undergo malignant degeneration. A definite diagnosis can be made only when the tumor can be seen through a proctoscope, or after it has prolapsed externally. At operation, an excision may be done if a positive diagnosis can be made.

Over 50 per cent of these lipomas were found in individuals between forty and sixty years of age. Lipomas in other parts of the body are found during

the same period of life. At this time in life there is an increased activity in the growth of general adipose tissue, which is of diagnostic importance, since the time of appearance of these growths coincides with that of carcinomas.

The treatment is surgical removal, in 1 or 2 stages. A cecostomy may be done as the first stage and a resection as the second. The Mikulicz operation is probably the procedure of choice for tumors of the transverse, descending, or sigmoid colons. Lipomas of the rectum may be resected through a proctoscope.

The author reports 1 case in detail.

JOSEPH K. NARAT, M.D.

**Dennis, C., Buirge, R. E., and Wangensteen, O. H.: An Inquiry into the Functional Capacity of the Cecal Appendage in Representative Birds and Mammals.** *Surgery*, 1940, 7: 372.

The authors continue their commendable investigations of the obstructive factor in the production of appendicitis.

Experimental studies were made of the absorption and secretion of fluid by the cecum, and cecal appendage when present, in the duck, goose, chicken, pigeon, dog, fox, raccoon, bear, skunk, cat, tiger, rabbit, squirrel, ground squirrel, rat, porcupine, hog, sheep, calf, marmoset, ring-tailed monkey, macaque, gibbon, chimpanzee, and man.

The rabbit, gibbon, chimpanzee, and man possess a cecal appendage. In all of these but the gibbon, fluid secretion by the appendix is sufficiently greater than fluid absorption to produce an increase in intraluminal pressure adequate to cause gross and microscopic evidence of acute inflammation.

In all animals which do not possess a cecal appendage, and in the gibbon, fluid secretion in excess of absorption was not observed.

The authors conclude that increase in the intraluminal pressure secondary to obstruction of the appendiceal lumen is probably an important factor in the etiology of acute appendicitis.

EDWARD W. GIBBS, M.D.

**Fana, C.: Anatomicoclinical Contribution to the Study of Mucocele of the Appendix** (Contributo anatomo-clinico allo studio del mucocele appendicolare). *Clin. ostet.*, 1940, 42: 2.

The author cites a case of mucocele of the appendix which had its origin in a simple inflammatory process of the appendix at the cecal insertion, and in which the background was quite characteristic of a chronic interstitial inflammatory process. It seems probable that the process began as an endotyphlitis and that bacterial toxins or attenuated bacteria penetrated the covering epithelium of the tissues surrounding the base of the appendix. The resultant hyperproduction of mucosa and reparative connective-tissue processes finally blocked the appendiceal lumen.

After studying some of the cases in the literature, the author wishes to reserve the term "peritoneal pseudomyxoma" for those cases originating from implants of the contents of cystomas of the ovary. He interprets the reaction to mucus from an appendiceal mucocele as being a form of hyperplastic peritonitis.

FRANK MCDOWELL, M.D.

**Filippini, G.: Studies on the Rôle of Retractile Sigmoiditis in the Production of Volvulus** (Ricerche sperimentali sul valore della mesosigmoidite retrattile nel determinismo del volvolo). *Sperimentale*, 1939, 93: 531.

The author analyzes the anatomical changes of the sigmoid loop and associated mesentery predisposing to the formation of volvulus, and lists them as follows: (1) those referable to the gut (segmentary redundancy and megasigmoid); and those referable to the mesentery (abnormal adhesions and ligamentous bands, anomalies of insertion, and a retractile mesosigmoid). After discussing the implications of these factors and reviewing the work of other investigators, Filippini reports a series of experiments performed on rabbits in which a condition similar to retractile mesenteritis was artificially produced and the results were studied. In each animal a large collecting vein which was seen to drain the extreme superior margin of the mesenteric insertion was isolated and tied off below the anastomotic arch, care being taken not to disturb the artery. Following this 1 c.cm. of aluminum silicate was injected between the layers of the mesentery, the material being distributed insofar as possible at the base of the mesentery. Finally, the two ends of the loop were lightly approximated and the insertions loosely joined by a ligature made with a human hair suitably sterilized. Twelve rabbits, divided into 2 groups, were treated in this manner; in the second group, however, the injection of silicate was omitted, as well as the approximation of the ends of the loop. In this control group, in which only the vein had been ligated and the histological picture of mesenteric congestion alone was produced, no volvulus developed, and no signs of obstruction were observed. In the other 6 experimental animals, retraction of the mesentery resulted; in 3 cases this closely resembled the mesenteritis noted in volvulus occurring spontaneously in the human being. It was concluded, therefore, that although volvulus does not appear constantly when inflammatory retraction of the mesentery is present, it does so in a high percentage of cases. The factors of redundancy and megasigmoid were thought to be of minor importance, although of a definite predisposing value. The approximation of the extremities of the loops was also indisputably of importance in the production of the lesion, but it was not effective alone. It was noted that volvulus never occurred before the fifteenth or twentieth day, at which time the inflammatory process in the base of the mesentery was well organized, the natural elasticity was markedly impaired, and the vascular supply of the loop was embarrassed. Retraction and fibrosis of the sigmoid mesentery was therefore believed a primary cause of volvulus.

EDITH FARNSWORTH, M.D.

**Cattell, R. B., and Swinton, N. W.: The Diagnosis and Treatment of Sigmoidal Polyps.** *New England J. Med.*, 1940, 222: 535.

Although considerable attention has been given to cancerous lesions of the large bowel in recent years and the principle of radical removal has been accepted as the method of choice, insufficient attention has been given to intestinal polyps or premalignant lesions.

Cattell discusses his experience with 10 cases of sigmoidal polyps. During this same period of the past seven years, there were 156 patients with polyps of the rectum and colon who were treated. During this same period 827 patients were operated on for carcinoma of the colon or rectum. A careful study of the removed lesions showed that 120 (14 per cent) could be proved histologically to have arisen from benign mucosal polyps. All stages of cellular change incident to the development of true carcinoma could be demonstrated in the various polyps removed. The frequent development of cancer in patients with congenital polyposis of the colon has long been known.

Bleeding was the presenting symptom in all 10 cases with sigmoidal polyps. In 6 instances the bleeding had been present for from one to fifteen years. One patient had obstructive symptoms because of the size of the polyp. Proctoscopic and sigmoidoscopic examination prove of the greatest value diagnostically. It is important to have the patient in the inverted position so that the rectosigmoid will become straightened by gravity and the instrument can be passed into the lower sigmoid. Barium enema and double-contrast air enema will often be necessary to demonstrate the discrete polyp. Repeated examinations may be required.

The treatment of rectal polyps is a relatively simple problem. Those below the pelvic peritoneal reflection can be fulgurated under direct vision; all polyps in any part of the large bowel should be destroyed or removed. Those above the pelvic peritoneal reflection can be fulgurated successfully if great care is exercised to avoid perforation and bleeding.

The treatment of polyps of the sigmoid is a more serious problem. Cattell believes that all sigmoidal polyps should be removed by laparotomy. Thorough examination of the entire colon should be routine. Polyps can often be palpated through the sigmoidal wall and moved back and forth through the lumen. Induration or fixation of the polyp makes the diagnosis of cancer and demands resection. After carefully walling off the segment of involved bowel containing the polyp, a longitudinal incision 3 in. long is made in the tænia-coli band. The polyp is excised with a generous portion of the mucosal base where the pedicle is free. The incision is next closed with fine silk sutures in two layers. In 4 of the 10 cases, the incision was reinforced with the appendices epiploicæ. In 1 instance the entire incision was made extraperitoneal by incising and reflecting a strip of lateral peritoneum.

Histological study of the 12 polyps removed from 10 patients by sigmoidotomy showed malignant adenoma in 1, adenocarcinoma in 2, while in 2 others there was a small focus of malignant change present in the polyp. In none was there any evidence of extension into the pedicle. In no case could cancer be determined from the gross appearance. The presence of early malignancy in 5 of the 10 instances furnishes striking evidence of the importance of removal of all sigmoidal polyps as soon as their presence can be demonstrated.

Postoperative convalescence was satisfactory in all cases, there being no complications and no mortality. One patient developed a carcinoma of the transverse colon distal to the hepatic flexure four and one-half years after the sigmoidotomy. This was removed by a modified Mikulicz type of resection. The 9 other patients remained well for the period of observation. JOHN W. NUZUM, M.D.

## LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

**Rosenberg, D. H., and Soskin, S.: The Azorubin-S Test of Liver Function; An Evaluation, with a Comparative Study of the Bromsulphalein and Hippuric-Acid Tests.** *Ann. Int. Med.*, 1940, 13: 1644.

Few tests of liver function have proved to be of much value in the diagnosis and prognosis of diseases of this organ because of the number of liver functions, as well as the great regenerative capacity and functional reserve of this organ. However, any test which might elicit information concerning a single function deserves study.

Azorubin-S, a dark red, stable, water soluble dyestuff of the mono-azo group, was first introduced as a substance suitable for the testing of hepatic function by Tada and Nakashima in 1924. They injected it intravenously and by duodenal intubation, and observed the color changes in the bile. In normal subjects as much as 95 per cent of the dye was excreted in the bile, the remainder being eliminated in the urine. Thus, renal disturbances can exert only a negligible influence upon its excretion by the liver. A delay in appearance of the dye in the bile or a prolonged urinary excretion was regarded as of pathological significance. The substance was found to be harmless and devoid of untoward effects, and when compared with 62 other dyes (bromsulphalein was not included in their study), yielded more reliable results.

The azorubin-S test is performed as follows:

After an overnight fast, a narrow flexible tube is passed into the duodenum and its position confirmed fluoroscopically. When bile begins to flow through the tube, 4 c.cm. of sterile 1 per cent aqueous solution of azorubin-S are injected intravenously. Five minutes later, 40 c.cm. of 25 per cent aqueous magnesium-sulfate solution are administered through the duodenal tube. The duodenal contents are collected in separate test tubes at one- or two-minute inter-

vals, and the time elapsing between the injection of the dye and the appearance of a very deep red efflux is designated as the "appearance time." For color determinations and comparisons the best results are obtained by observing the solutions in bright daylight; slanting the tube against a white background is also helpful.

In normal individuals usually a succession of color changes in bile was noted in the following order: orange, reddish-orange, light red, light cherry red, and deep cherry red, after which the color faded out in the reverse order. The appearance time of the significant test color (deep cherry red) ranged from seventeen to twenty-nine and one-half minutes, whereas the time elapsing before the first appearance of the dye, however faint, varied from eight to twenty-five minutes.

The technique of the azorubin-S test lends itself to a combined study of liver function and composition of the bile. The coexistence of cholelithiasis with hepatic cirrhosis is not uncommon, the reported incidence being as high as 13 per cent. Upper abdominal pain may be the predominating symptom in either disease, yet the finding of a non-visualizing gall bladder cholecystographically may be of no diagnostic significance in the presence of cirrhosis, which often leads to erroneous conclusions. In these cases the establishment of the presence of calculi, which is of importance therapeutically, may be impossible without a crystallographic study of the bile. A combined liver function test and bile examination is thus advantageous.

The azorubin-S test of liver function, which has received little attention in this country, was performed on 14 normal subjects; and a comparative study of this test with the bromsulphalein and hippuric-acid tests was made in 19 cases of cirrhosis, 2 cases of acute toxic hepatitis, 1 case of subsiding acute hepatitis, 1 case of fatty metamorphosis of the liver, and 4 cases of relatively early chronic hepatitis. The azorubin-S test was found to be as reliable as the bromsulphalein test and better than the hippuric-acid test in cases of cirrhosis, while in the cases of relatively early chronic hepatitis, the azorubin-S test was superior to both the other tests.

Although the azorubin-S test requires duodenal intubation, the method lends itself to a simultaneous crystallographic study of the bile.

MANUEL E. LICHTENSTEIN, M.D.

## MISCELLANEOUS

**Faxon, H. H.: Subphrenic Abscess.** *New England J. Med.*, 1940, 222: 289.

A series of 175 cases of subphrenic abscess is presented, and the anatomy of the subphrenic spaces is discussed. It is the author's opinion that a lack of familiarity with these constant anatomical spaces often leads to an unwise selection of approach for drainage and to an unfortunate hesitancy in the execution of an operation. The left subphrenic area is less commonly involved than the right, there being

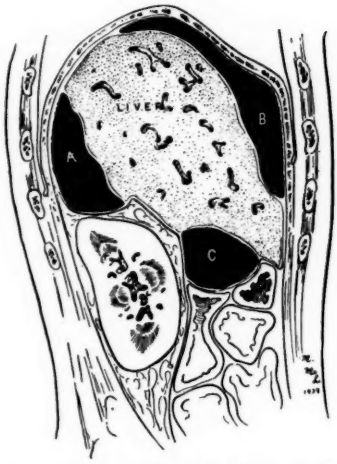



Fig. 1. Sagittal view of the right abdomen. This shows the relative sites of abscesses occurring in the three most commonly involved subphrenic spaces. A, right posterosuperior; B, right anterosuperior; C, right inferior.

only 13 per cent of this series in which an abscess was found to the left of the midline.

With reference to the cause, Faxon believes that a vast majority of subphrenic abscesses originate from an extension of intraperitoneal sepsis, although in some instances infection may occur by way of the lymphatics and the blood stream. In this series the origins of the infection were: the appendix in 31 per cent; the stomach and duodenum in 27 per cent; the liver and bile passages in 21 per cent; and the other sources combined in 21 per cent.

In the early stages it is not always easy to diagnose the condition of subphrenic abscess. In a case in which subphrenic abscess is a likely possibility, the diagnosis is made on one or more of the following points: the presence of tenderness upon firm palpation over the twelfth rib or lower costal margin; clinical findings of a high, fixed diaphragm on the affected side; pain referred to the shoulder or neck; hiccoughs, and discomfort on deep respiration; and confirmation by roentgenological studies. Faxon's statistics substantiate the statement that, regardless of the space involved, if the diaphragm can be visualized by x-rays it will almost invariably be found to be elevated and, usually, fixed. The author believes many physicians are inclined to neglect obtaining a satisfactory lateral roentgenogram or making adequate fluoroscopic studies, and he considers the evidence secured by these means of inestimable help. In 5 of the cases in this series the injection of a radiopaque substance into a sinus tract persisting from previous operative drainage demonstrated the location of a residual subphrenic abscess. The belief that the abscess must almost always be in direct contact with the diaphragm to

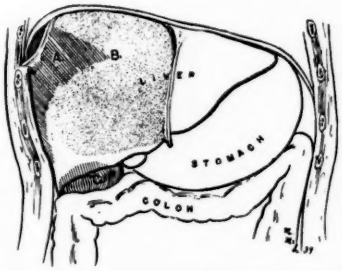



Fig. 2. Anterior view of the abdomen. This shows the relative sites of abscesses occurring in the three most commonly involved subphrenic spaces. A, right posterosuperior; B, right anterosuperior; C, right inferior. The shaded portions of A and C are actually not visible in this view as they lie behind the substance of the liver.

give pleural effusion above it is supported by the findings in this series. Downward displacement of the liver is held to be suggestive of an abscess in one of the superior spaces.

Pre-operatively, determination of the space or spaces involved can be accomplished by an observance of the following: location of the point of maximum tenderness; the x-ray findings; consideration of the original septic process; and aspiration of pus from a suspected area beneath the diaphragm. However, the author considers the latter a pernicious practice that should be condemned. Thoracentesis of the pleural cavity may be carried out to advantage in certain cases.

The treatment of subphrenic abscess lies in prompt drainage of the area. A discussion of the various methods of approach is given, and the author concludes that the retroperitoneal type is the safest, since the theoretical and statistical evidence favors it. Contamination of the pleural or peritoneal cavities at the time of operation more than doubles the mortality rate, and such contamination occurs far more frequently with the transthoracic and transperitoneal types of approach than with the retroperitoneal operation. EARL GARSIDE, M.D.

**Lehman, E. P., and Boys, F.: The Prevention of Peritoneal Adhesions with Heparin. An Experimental Study.** *Ann. Surg.*, 1940, 111: 427.

This contribution to the problem of peritoneal adhesions merits studious attention. As a means of prevention of peritoneal adhesions, the authors endeavor (1) to destroy fibrin and (2) to prevent its formation. They describe the manner in which an exudate on the peritoneal surface leads to adhesions: the exudate, serous or seropurulent, becomes fibrinous; the fibrin is then organized by connective-tissue and blood-vessel elements of the subserosa. This process always takes place in fibrin and cannot occur without fibrin. It is claimed that heparin prevents the formation of fibrin in the blood. Based upon this hypothesis, the authors conducted various experiments. They state, "Heparinization of animals and man, in vascular surgery, to an extent that is effective in preventing thrombosis, has not been found to be hazardous from the point of view of wound hemorrhage, if complete hemostasis is obtained at the time of closure."

Their report includes the protocols of 56 rabbits, 30 dogs, and their controls.

Two sets of experiments were carried out with corresponding controls, one with rabbits and one with dogs. In rabbits, the adhesions were produced by mechanical damage and by bacterial contamination. The adhesions were then separated and the degree of their re-formation observed. All surgery was performed upon rabbits anesthetized by local infiltration with 1 per cent novocaine. The dogs were given ether intratracheally. Scrupulous asepsis and extreme gentleness were employed. Fine silk was used for the intraperitoneal ligature. The incision was made through an untouched area of the abdominal wall whenever a repeated survival celiotomy was indicated. Closure of the incision always avoided the exposure of cut surfaces and prevented suture material from presenting within the abdominal cavity.

RABBITS

*Adhesions caused by mechanical damage.* A pledget of folded dry gauze of constant dimensions was introduced close to the angle between the mesial surface of the cecum and the lateral surface of the ileum after light dry-gauze scarification of the underlying serosa. This was anchored by 2 fine silk serosal sutures. In from three to five days later the abdomen was opened and the pledget and sutures were removed. The animals were divided into 3 control groups and 1 experimental group.

In the first control group the abdomen was closed after separation of the adhesions without the intraperitoneal administration of any solution. In the second control group 25 c.cm. of normal saline solution were left in the peritoneal cavity, and in the third control group 25 c.cm. of amniotic fluid were administered intraperitoneally before closure.

In the experimental group 25 c.cm. of normal saline solution containing 750 units of heparin (30 mgm. per cent) were injected into the peritoneum. The injections in all groups were repeated by paracentesis on the first and second postoperative days. One week later all animals were examined for the presence or absence of adhesions.

*Adhesions caused by peritoneal contamination.* At the first operation the appendix was perforated near the tip and its contents were smeared over adjacent serosal surfaces. Also, various solutions were injected intraperitoneally in spite of an unclosed opening of the appendix. All experiments were carried out as noted, except in the amniotic-fluid control group.

DOGS

*Adhesions caused by peritoneal contamination.* The treatment of the appendix in dogs was the same as that carried out in rabbits. Forty per cent of the

dogs died from peritonitis and 11 per cent developed localized abscesses; these dogs are not included in this report. Six weeks later the abdomen was opened and the resulting adhesions were counted and carefully and completely divided by sharp dissection. Bleeding was controlled by hot packs or by fine-point ligation with silk. At this time, as in the rabbits, 3 control groups and 1 heparin experimental group were established. One hundred cubic centimeters of normal saline, 100 c.cm. of amniotic fluid, and 100 c.cm. of heparin solution (3,000 units) were introduced into the peritoneal cavity of the proper groups, respectively. Injections were repeated by paracentesis on the first and second postoperative days. Two weeks later re-formation of the adhesions was observed and a count was made at a final celiotomy. In counting the adhesions in dogs, a continuous adhesive band or sheet was considered as a single adhesion. In most instances these probably represented the fusion of many smaller adhesions.

In rabbits, after mechanical peritoneal trauma, there was a striking difference between the numbers of adhesions in the controls and in the animals treated with heparin. The controls yielded adhesions in 100 per cent, while the experimental group (heparin) yielded adhesions in only 10 per cent. Adhesions after peritoneal contamination in the control groups amounted to 100 per cent; the experimental groups (heparin) yielded no adhesions.

The results in dogs were not so good. In 20 controls the average number of adhesions, divided two weeks later, amounted to 8 per cent. The average number of adhesions which re-formed two weeks later amounted to 12.6 per cent (157 per cent). In 10 dogs in the experimental group, the average number of adhesions which were divided, amounted to 9.7 per cent; the average number of adhesions which re-formed was 2.6 per cent (26 per cent).

It was a striking observation that normal saline-solution injections resulted in more than twice the usual number of adhesions.

The coagulation time of the blood (determined by capillary-tube method) in dogs following the intraperitoneal injection of heparin was lengthened to ten minutes, two hours after injection, and lasted about eight hours. A rapidly developing polymorphonuclear leucocytosis appeared in dogs during the first twenty-four hours after heparin injection. Twenty-four dogs developed massive intra-abdominal hemorrhage from which they died; one of these died of paralytic ileus.

Although the number of experiments is inadequate for positive deductions, there can be no doubt that heparin has proved to be astonishingly effective in preventing adhesions. As yet, research does not warrant the application of heparin treatment to patients, but future developments, it is hoped, will permit clinical application.

The authors conclude that heparin introduced into the peritoneal cavity of the dog and the rabbit is effective in preventing the formation and re-formation of adhesions. MATHIAS J. SEIFERT, M.D.

# GYNECOLOGY

## UTERUS

**Koeberle, F.: Internal Adenomyosis of the Uterus with Tuberculosis** (Ueber Adenomyosis uteri interna tuberculosa). *Wien. klin. Wchnschr.*, 1939, 1: 122.

In the world literature there are, up to the present, 21 established observations of adenomyosis of the uterus with simultaneous tuberculosis. The ideas concerning the combined appearance of both diseases vary. While some assume a coincidental occurrence of both diseases, others believe in a secondary infection in a predisposed patient. Robert Meyer and Schottlaender are of the opinion that the uterine adenomyosis is the sequel of tuberculous infection.

The author's case concerns a forty-six-year-old married woman who had twice given birth and who had twice aborted. After unsuccessful curettage because of long continued irregular bleeding, in the presence of histologically proved mucous-membrane tuberculosis, the uterus and both adnexa were surgically removed. The anatomical study of the operative specimen showed a combination of adenomyosis and tuberculosis in the uterus with a healed tuberculosis of the right tube. On the basis of the local association of the two processes a causal connection of both diseases was assumed, in the sense that in the presence of a tendency toward adenomyosis changes in the endometrium the tuberculosis was the exciting cause for the internal adenomyosis of the uterus. (Huber). John R. Paine, M.D.

**Fricke, R. E., and Bowing, H. H.: Radium Treatment of Carcinoma of the Cervical Stump.** *Am. J. Roentgenol.*, 1940, 43: 544.

Carcinoma of the retained cervix, subsequent to a supravaginal hysterectomy, is a very serious condition. When discovered most of the lesions are in advanced stages and the prognosis is poor. This condition occurs at the time of the menopause, or slightly later, and occurs most often after a subtotal hysterectomy for uterine fibromyomas. Undoubtedly, as Branscomb has suggested, when uterine myomas are known to be present in cases of vaginal bleeding, investigation of possible causes of vaginal bleeding other than uterine myomas may not be considered, and a coincidental cancer of the cervix may be easily overlooked.

For the surgeon who must decide between performing a subtotal hysterectomy and a panhysterectomy when removal of the uterus is necessary, acquaintance with the true incidence of cancer in the cervical stump is of vital importance. Unfortunately, this information is difficult to obtain. The follow-up of cases by surgical clinics yields a very low incidence, which is natural when it is remembered that patients may have to be traced for two or three decades. Radiological clinics, in the treatment of carcinoma of the cervix, have found a far higher incidence of malignancy in the retained stump than have surgical clinics.

From the experience among 1,676 patients who had carcinoma of the cervix treated with radium at the Mayo Clinic from 1915 to 1930, inclusive, the condition of 108 was diagnosed as carcinoma of the cervical stump. By eliminating a few patients who were not treated at the clinic or who received treatment by cauterization only, 99 cases remain, 6.4 per cent. However, further pruning was necessary. The authors agree with Nuttall and Todd, and with Sharples, that if two years or longer have elapsed between subtotal hysterectomy and the discovery of the malignant lesion in the retained cervix, the lesion is probably a true carcinoma of the cervical stump, and not a "coincident" or dual carcinoma which was present before the operation was performed.

On this basis, 57 cases remained, or 3.4 per cent of the total series. The interval between operation and the diagnosis of malignancy was more than twenty years in 5 cases, and between ten and twenty years in 15 additional cases.

It was found, on analysis, that careful radium and roentgen therapy does yield worth-while results, which have been improving with changes in technique. Cure for more than five years was obtained in 26.3 per cent of the cases. The patients are now living and well nineteen, seventeen, sixteen, and twelve years, respectively, after their last treatment, although the extent of the lesion on diagnosis had represented an advanced stage (80 per cent were in Stages 3 or 4) and the grade of the cancer was high in cases in which biopsies had been taken (75 per cent were Grades 3 or 4). Incidentally, patients who have never been pregnant are not immune to cancer of the cervix. In 21 per cent of cases in our series a history of non-fertility was obtained.

Results were not so fortunate in the "coincident" cases, or dual malignant lesions, those discovered less than two years after operation with carcinoma probably coexisting at the time of the operation. As Nuttall and Todd had emphasized, results in these are comparable to the results of incomplete operation for a malignant lesion anywhere in the body. Although the five-year survivals in the authors' series were only 5 per cent less (21.4 per cent), more than half of the members of the group died within the first year after treatment (54.8 per cent), contrasted with 22.8 per cent of the patients in whom true carcinoma of the stump was present. The lesions were more advanced when first seen; only 7 per cent were in Stage 2, while in the group with true carcinoma of the stump 20 per cent were in Stage 2.

Hence, although in the presence of carcinoma of the cervical stump careful irradiation can accomplish much and the prognosis is not utterly bad, much remains to be accomplished in the way of prevention. The seriousness of carcinoma of the

cervical stump must be publicized and re-emphasized. Whenever a subtotal hysterectomy is performed, a conscientious examination of the cervix should be made. After such an operation, the patient should have pelvic examinations at stated intervals, and should be instructed to come voluntarily for attention at any time, if vaginal bleeding occurs.

## ADNEXAL AND PERIUTERINE CONDITIONS

**White, M. M.: The Effect of Follicular Hormone on Non-Patent Fallopian Tubes.** *Brit. M. J.*, 1940, 1: 342.

The author reviews briefly the studies of Clauberg on the effect of estrin on the fallopian tubes. By histological examination of sections of fallopian tubes taken from women who had undergone a course of estrin therapy before being operated upon, it was shown that hyperemia and proliferation of tubal epithelium had occurred.

Experiments along these lines were carried out by the author. A total of 13 women was studied. In 9 of the 13 women, lipiodol was injected into the uterus and on x-ray examination non-patent fallopian tubes were found. In 7 of these, the x-ray diagnosis of non-patency was confirmed by insufflation with Rubin's test. In the 4 other patients who were treated, there was no injection of lipiodol before estrin therapy was started. Two of these had non-patent tubes at a pressure of 200 mm. Hg and 2 had patent tubes at a pressure of 180 mm. Hg.

Each of the 13 patients was then given five injections of 50,000 I. B. U. of estradiol benzoate at five-day intervals, and the insufflation was repeated. In all of these women other investigations and the past histories gave no cause except non-patency of the fallopian tubes as a possible reason for sterility on the part of the woman.

Of the 7 patients in whom non-patency of the fallopian tubes was confirmed both by roentgenography and insufflation, 4 acquired patent tubes, 3 with good tubal contractions and 1 with poor contractions. Three of these women became pregnant, 2 miscarrying at six weeks. Patency and good contractions resulted in only 1 of the 2 patients in whom the tubes were shown to be non-patent on insufflation only. In 3 of the 4 patients in whom the tubes were patent only at high pressure and showed no contractions, the tubes became patent at a lower pressure and showed contractions, but the contractions were good in 1 instance only. The patients most likely to respond to treatment are those in whom the tubal obstruction is at the fimbriated end.

HERBERT F. THURSTON, M.D.

## EXTERNAL GENITALIA

**Raso, M.: Congenital Cysts of the Vagina** (Cisti congenita della vagina). *Arch. di ostet. e ginec.*, 1939, 3: 528.

The infrequency of the occurrence of vaginal cysts is indicated by the fact that until 1933 Castagna was able to find only 340 cases in the literature, and since then the author has added 20 more, which makes a total of 360 cases to date. Vaginal cysts, usually single but sometimes multiple, vary in size from that of a hazel nut to that of a turkey's egg, and occur at all ages. These cysts, which usually contain blood, mucus, and serum, may be located in any part of the vagina. Their genesis, in most cases, is obscure. Prognosis is always good; only in 1 case was there malignant degeneration (Falkener, 1903).

The author discusses the various classifications that have been suggested, but prefers the simple classification of Polizzotti, i.e., congenital (wolffian and muellerian ducts); acquired (traumatic and inflammatory); and mixed.

The embryonic development of the uterus and vagina and the parts from which they are derived are discussed in order to present a clearer understanding of the formation of the muellerian cysts.

Cysts originating from the wolffian duct are found with greater frequency in the fetus and newborn and represent about 40 per cent of all vaginal cysts. Muellerian cysts are located in various parts of the vagina but occur most frequently in lateral positions and are never above the fornix. The stratified epithelium is evidence of the derivation of the cyst from the muellerian duct.

The author reports a case of vaginal cyst of muellerian origin in a fetus. Only 7 such cases have been reported in the literature. The cyst, which was the size of a pea, was located at the angle between the entrance and the right fornix.

The author discusses all the theories of mechanism of formation of the cysts of the muellerian duct. Nurberger believed that the formation of muellerian cysts was based on three mechanisms: isolation of the tract of the muellerian duct; deficient fusion of two muellerian ducts with permanency of the residue of one duct; and postfetal detachment of vaginal epithelium. To these the author adds two more mechanisms: interflexion in the primitive period of development of the deep epithelium of the vagina with successive detachment of the original surface and distention of the interflexed cavity; and the possible detachment of the cysts of the vaginal gland derived from the uterus.

The author believes, after having reviewed the genesis and theories of mechanism of formation, that cysts are formed by epithelial interflexion of the mucosal tract of the fornix probably in the period of development which precedes the separation of the epithelial lamina.

MICHAEL DEBAKEY, M.D.

**Mosto, D., and Radice, J. C.: Tumors of the Vulva, Benign and Malignant. Histopathology and Discussion of 34 Primary Tumors** (Tumores de vulva, benignos y malignos. Histopatologia y consideraciones sobre 34 casos de tumores primitivos). *Rev. de med. y ciencias afines*, 1939, 1: 33.

Tumors of the vulva are of interest because of their relative scarcity as compared to the incidence

Fig. 1

Fig. 1. Myxomatous vascular structure of a pedunculated fibromyxo-angioma of the labia majora.

Fig. 2

Fig. 2. Reticulosarcoma of the vaginal vestibule.

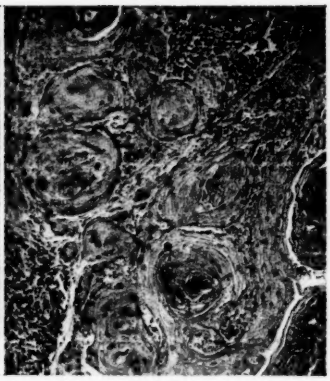


Fig. 3

Fig. 3. Spinocellular epithelioma of the clitoris.

of other tumors; because histological study always is available and gives a precise knowledge of the anatomical nature of the tissue; and because their accessibility permits satisfactory treatment with a great possibility for cure. The author presents the results of his studies on 34 primary tumors of the vulva studied at the Rawson Hospital. Emphasis is placed on the histopathology. The sites of predilection of these tumors are the following, in diminishing order: labia majora, labia minora, Bartholin's glands, urethral caruncle, clitoris, and vestibular bulb. The most varied types of tumors, both benign and malignant, occur on the vulva.

The authors then present a detailed classification and tabulation of primary tumors of the vulva under the broad groups: connective-tissue tumors, epithelial tumors, and complex, mixed tumors. They discuss the benign tumors and note that they are encapsulated, do not form metastases, evolve slowly, and interfere with coitus, micturition, and walking. They may be single or multiple, superficial or deep. The average age of the patients is thirty-five years, with extremes of fifty-two and five years. Microscopically the most common benign tumors in order of diminishing frequency are: fibromas, adenomas, papillomas, and cysts. The period of development of these tumors varied from five months to ten years. It is pointed out that certain fibro-adenomas resemble certain tumors of the breast, such as juvenile fibroadenoma. Morphologically these may be derived from certain sweat glands which have an embryological origin similar to that of the mammary gland. The various benign connective-tissue and epithelial tumors are described in great detail with numerous references to the literature, and photomicrographs.

The malignant tumors are comparatively rare as compared to the incidence of malignancy in other parts of the body. The frequency of incidence is, according to Gossel, 5.1 per cent; and according to Matmuller, 3.2 per cent. Secondary malignancy of the vulva is most rare. In the authors' series there were 11 benign and 23 malignant tumors. These tumors occur at an advanced age and are commonly associated with pruritus and pain. The favorite locations of malignancy of the vulva in order of frequency are: the labia majora, the clitoris, the vestibule, and Bartholin's glands. Leucoplakia is frequently associated with malignant tumors. The only case of glandular epithelioma probably developed from the remains of an aberrant mammary gland and looked like an adenocarcinoma.

Biopsy is indicated as an important aid in establishing the diagnosis and directing the proper course of treatment. JACOB E. KLEIN, M.D.

**De Godoy, P., and Delascio, D.: Giant Papilloma of the Vulva** (Papilôma gigante da vulva). *Rev. obst. e ginec. de S. Paulo*, 1939, 3: 347.

De Godoy reports a case of giant papilloma of the vulva which was excised, and discusses vulvar papillomas in general. Clinically, the lesion is called acuminate condyloma, but anatomopathologists call it papilloma; as the clinical concept should be based on the anatomicopathological examination, the author accepts the term "papilloma."

Papilloma occurs frequently, but its cause has not yet been established. Some authors incriminate gonorrhea or any other infection which causes chronic irritation; others accuse various spirochetes, or ordinary saprophytes. Some claim that papilloma is contagious and others that it is inoculable; a filtrable virus has been accepted by Serra. Even psychic influences have been cited. A theory of trophic disturbances has been proposed as favoring the development of papilloma, while hormonal disturbances have been suggested as a factor because papillomas are frequent during the menacme and rare during childhood and after the menopause.

Papillomas occur in the vicinity of the vulva and especially on the small and large labia and may invade the vagina and the cervix. They are nearly always multiple and vary in size; their color is light pink or wine red; they are soft and humid or dry. Histologically, they present a connective-tissue vascular stroma and a covering of stratified pavement epithelium. They may be complicated by ulceration and hemorrhage, infection, or cancerous degeneration; the possibility of the latter is denied by some authors.

The subjective symptoms are generally discreet and determine no mental reaction in the woman, perhaps because papilloma occurs chiefly in those of low culture and poor intellect. In some cases, a discharge, pain, or pruritus develops and leads to medical examination. The diagnosis is easy, but a histological examination should always be made. The intradermal reaction with specific antigen and the complement deviation test have been studied by Maderna; they were always negative. The differential diagnosis includes condyloma planum and carcinoma.

With regard to prognosis, papillomas are likely to be benign, but the possibility of cancerous degeneration must not be overlooked. The treatment consists generally of cauterization or surgery. Numerous treatments have been recommended. The physical treatments are general or local. The general treatments are intended to modify the terrain by means of magnesium salts, arsenic, autohemotherapy, intracutaneous injections of milk, and the intravenous administration of glycerin diluted with isotonic serum. The local treatments are chemical (chromic, acetic, nitric, salicylic and oxalic, or carbolic acids; or silver nitrate, iron perchloride, or ethyl chloride); physical (ultraviolet rays, thermocautery, diathermocoagulation, and radium); or surgical. Psychic treatment has been recommended.

Papilloma often occurs during pregnancy, which constitutes an undoubted predisposing factor. Small tumors may be cauterized, but large ones should be left alone until after delivery; however, giant ones which would interfere with delivery must be removed even at risk of abortion. RICHARD KEMEL, M.D.

## MISCELLANEOUS

**Browne, O'D.: Ovarian Dysmenorrhea: Its Etiology, Diagnosis, and Treatment.** *J. Obst. & Gynaec. Brit. Emp.*, 1939, 46: 962.

This article was written to draw attention to the part played by the ovary in certain cases of dysmenorrhea. Most current classifications of dysmenorrhea regard the uterus as the only possible etiological factor and do not consider the rôle that may be played by the ovaries, fallopian tubes, or other structures. Dysmenorrhea of ovarian origin is a definite entity, but it may often be accompanied by characteristic uterine discomfort, a fact which makes the separation of the two possible sources a matter of the greatest difficulty.

To agree that ovarian dysmenorrhea can exist either as an individual complaint or in conjunction with menstrual pain of uterine origin implies the acceptance of the view that the two structures possess their own independent and separate nerve supplies, and this is now believed to be true. Ovarian innervation is bilateral, and pain originating in one ovary may be referred to that side, or to the opposite side, or to both the affected and the opposite sides.

It has been shown that pathways for painful ovarian stimuli exist in the ovarian nerves, as is known to be the case in the presacral system in connection with the uterus, and the success of the operation of ovarian denervation for the block of painful ovarian stimuli depends upon this fact.

Only the painful or tender, though apparently normal, ovary is considered, the frankly diseased, adherent, and inflamed or enlarged organ, as found typically in secondary dysmenorrhea, being excluded. The grossly diseased ovary is readily recognized and accepted as a source of pain, but it is unusual in the young patient in whom the typical symptoms under discussion exist.

Sclerocystic changes assume by far the greatest importance in the cases under consideration and were present in all the cases of ovarian dysmenorrhea. The French School supports the neurogenic etiological theory, and believes that sclerocystic ovarian changes are secondary to the influence of some ovarian-nerve lesion rather than a primary condition. If we accept the neurogenic theory of sclerocystic ovarian degeneration with its coincident ovarian-nerve lesions, we can readily understand that only certain ovaries will be painful, and why it is that pain is an unusual symptom in the many and various sized ovarian cysts encountered. In this way also it becomes apparent how mittelschmerz and ovarian discomfort or pain may be totally absent in most women, but is often present and excessive in the minority whose ovarian nerves are abnormal. The two determining factors productive of excessive ovarian pain would, therefore, appear to be an existing nerve degeneration, and pressure upon either the ovarian intrinsic nerves or some of their fibrils near the granulosa-cell layer of a follicle. Such pressure could be constant from excessive fibrosis in the proximity of nerve endings, or periodic from the edema which is present at the times of ovulation and the premenstrual phase.

Although ovarian pain is at first localized, it often becomes distributed to the superficial areas supplied by cutaneous nerves originating from the tenth thoracic segment and supplied by the genitofemoral nerve. Iliac-fossa pain on the left side is accepted as suggestive of ovarian disease of that side. Opinion generally is agreed upon the sub-umbilical localization of the pain. Winter described ovarian pain as typically "radiation to the hips and thighs on pressure over the ovaries." In brief, ovarian pain may be unilateral, bilateral, or referred to the side opposite to the lesion; menstrual, but chiefly premenstrual; always sub-umbilical, but chiefly on the

left side and radiating down the thighs. Although not included in the list, nausea is regarded by some as a constant symptom, while dyspareunia, dyschezia, and syncope are said often to be present.

Accurately defined midline lower abdominal pain must be regarded as uterine in origin and should not be confused with the ovarian type. Diffuse lower abdominal pain in all probability indicates dysmenorrhea of coincident uterine and ovarian origin. Ovarian pain also appears typically in two or three premenstrual days, rarely persists after the onset of the flow, and often disappears some considerable time before the bleeding begins. It can be faithfully reproduced by evoking the "deep sensibility reflex" of the ovary by pressure upon one or both ovaries during bimanual examination. Radiation down the thighs (the viscerosensory reflex) can be elicited sometimes in this way.

In contrast, uterine pain may only begin with the flow and cease after an hour or two or persist until the bleeding has completely ended. It is frequently sharp, stabbing, cramplike, or colicky in character (the so-called "spasmodic" dysmenorrhea) and can be reproduced by passing a uterine sound.

Only severe cases of dysmenorrhea are considered in this communication. By a severe case the author means a patient who suffers so much pain that her work or normal activity is interrupted every month, however much she tries to make the least of the pain. After a routine general examination to exclude extragenital complaints which might upset the menstrual function, a thorough bimanual examination is carried out, with accurate ovarian palpation and the passing of a uterine sound when possible.

If a reasonable degree of bimanual compression of the ovaries, or slight displacement of them within the pelvis, produces pain similar to that experienced at menstruation, an ovarian origin for the menstrual pain may reasonably be suspected. The character and localization of the pain produced by ovarian compression is compared with that produced by passing the uterine sound. By comparing these two pains evoked by examination with the patient's account of her menstrual pain, it is usually possible to decide whether the dysmenorrhea is of uterine origin, ovarian origin, or partly due to ovarian and partly due to uterine stimulation.

Medicinal treatment has now been abandoned when severe ovarian dysmenorrhea is suspected as it has proved itself unsatisfactory in such cases. For the same reason hormonal therapy is inapplicable.

Cervical stenosis was present in only 1 or 2 per cent of the women under investigation. The author believes that cervical stenosis is rarely a cause of dysmenorrhea and that dilatation of the os is therefore illogical treatment.

Medicinal treatment of dysmenorrhea with alcohol, morphine, and other habit-forming drugs should be avoided, while the value of tonics, improved hygiene, exercises, heliotherapy, and psychotherapy are sometimes helpful. Organotherapy is only likely to be helpful in dysmenorrhea of uterine origin.

Presacral sympathectomy cannot possibly relieve pain of ovarian origin, but in the author's opinion it is efficacious treatment for dysmenorrhea of uterine origin.

In 1927 L'Hermitte and Dupont suggested that the painful ovary could be rendered insensitive by denervation. These observers realized that a therapeutically successful denervation was necessarily bilateral. Their most recent technique, in brief, is the division of the two or three main ovarian-nerve bundles in the mesovarium without interference with the ovarian blood vessels.

The author's present technique for bilateral ovarian denervation consists of bilateral division of the infundibulopelvic ligaments and their nerves and blood vessels, at the brim of the pelvis through a midline lower-abdominal incision. Under general anesthesia, divided ends of each ligament are securely ligated with fine silk ligatures, and the cut ends of each ligament are sutured together on each side with two fine catgut stitches to prevent subsequent elongation of the ligament and ovarian prolapse. It is most important to divide each infundibulopelvic ligament close to its ovarian attachment, as in this way no nerve fibers will escape. It was found that interruption of the blood supply of the ovary need not be feared.

When necessary to correct a uterine misplacement a Gilliam suspension is performed, and the appendix is removed only when it is inflamed or adherent.

*Results following bilateral ovarian denervation.* Eighteen patients were selected as suitable for bilateral ovarian denervation. Sixteen women have been followed up satisfactorily. Ten of these regard themselves as completely cured. Of these women the only 2 who have married since their operation both have now normal healthy infants. Labor in each case was normal and ended spontaneously. We may regard the 10 patients who were completely cured by bilateral ovarian denervation as examples of true ovarian dysmenorrhea, and consequently assess its incidence as 11.9 per cent of all severe dysmenorrheas.

Ovarian dysmenorrhea often occurs in association with uterine dysmenorrhea constituting the cases the author terms "mixed dysmenorrhea." In the light of this knowledge the partial and complete failures (35 to 40 per cent) Cotte and others have experienced following presacral sympathectomy are readily understood, as is the persistence of dysmenorrhea following total hysterectomy. Polycystic ovarian changes with sclerosis were a constant finding in all the patients successfully treated. The menstrual rhythm was usually normal despite the pre-existing ovarian abnormality.

Six cases are classified as failures. Four of these showed gross pelvic lesions which were not diagnosed before operation. Incorrect diagnosis and treatment may be regarded as the explanation of these failures.

The 2 remaining failures, in which a gross pelvic lesion was not present, appear to have resulted from a wrong choice of treatment (ovarian denervation

alone) as the degree of uterine pain was underestimated. DANIEL G. MORTON, M.D.

**Westman, A.: Differential Diagnostic Problems in Virilizing Diseases of Women** (Differentialdiagnostische Probleme bei virilisierenden Erkrankungen der Frau). *Acta obst. et gynec. Scand.*, 1939, 19: 455.

Westman discusses some differential diagnostic problems with reference to 3 cases.

The first case was that of a woman aged thirty-seven with the typical features of Cushing's disease. She had a full-moon face, marked adiposity of the trunk, slender extremities, striæ, marked growth of hair on the upper lip and chin, reduction of the mammary glandular substance, psychically marked dullness, and blood pressure of 170/100. She had had multiple rib fractures, which were healing with callus. Exploration of each adrenal gland revealed no abnormality. Roentgenographic study of the skull showed no hypophyseal changes, but spotty reduction of the bone shadow. Treatment consisted of irradiation of the hypophysis, and was followed by some improvement. The author discusses the various theories on the cause of Cushing's disease, and mentions that some authors disagree with Cushing as to the importance of the basophile adenoma. Biopsy in the author's case, however, did not support the assumption of the adrenal disturbances as the cause of the syndrome, and the fairly good result of the irradiation of the hypophysis pointed to this gland as governing the condition.

In the second case a woman of twenty-six years developed similar changes to those in the first case, except for the striæ and the osteoporosis which were missing. After estrone treatments had not helped her, the author investigated the condition of the adrenal glands by biopsy. The left one was found to be normal, while the right had been transformed into a tumor of about 8 by 9 by 5 cm. which partly embraced the vena cava. This tumor was removed. After a few hours the blood pressure fell alarmingly, and in spite of intravenous drip, cortin, ephedrine and cardiac stimulation, the patient died about twenty-four hours after operation apparently from adrenal insufficiency. Post-mortem examination was essentially negative. Histologically the tumor was diagnosed as a cortical adrenal adenoma of a benign character. As the left adrenal gland was almost normal histologically, Westman explains the fatal adrenal insufficiency by assuming that the apparently normal left gland was in a state of hypofunction because of the large tumor of the other gland. When this was removed, the presumably healthy gland on the left side failed to substitute. The hypophysis was found to be entirely normal, and also the hyalinization of the basophile cells, typical for Cushing's disease according to Crooke, was absent.

The third case was that of a girl of sixteen who had never menstruated except for one day when she was thirteen. She had a deep bass voice, virile type of hair distribution, very small breasts, and a marked beard on the chin and cheeks. The clitoris was enlarged, the uterus very small, and there was a resistance behind it of the size of an orange. Hormone estimation and roentgenograms of the sella region were normal. The diagnosis of a virilizing ovarian tumor was made and affirmed on operation. Oophorectomy and salpingectomy were done on the left side. The tumor weighed 70 gm., and its dimensions were 8 by 9 by 4 cm. Histologically it resembled an arrhenoblastoma. After operation some of the masculine features (amenorrhea, undeveloped breasts, beard) disappeared, while others (voice, hypertrophied clitoris, hair distribution) persisted. As the left adrenal gland had been found enlarged on operation, the author believes that there is still a persistent virilizing influence originating from this gland.

The differential diagnosis in cases of virilism in women is easy if there is a palpable ovarian tumor. As, however, even very small ovarian tumors, undetectable by bimanual palpation, may be responsible, an exploratory laparotomy often has to be done. This enables the surgeon to palpate the adrenals, and is a method which the author prefers to roentgenography following insufflation with air.
HEINRICH LAMM, M.D.

**Turunen, A.: External Endometriosis** (Ueber die Klinik der Endometriosis Externa). *Acta obst. et gynec. Scand.*, 1939, 19: 477.

This writer presents in a well organized manner a careful study of 200 cases of endometriosis. All of the cases were followed-up for at least one year. Based on the observation of 195 cases which were operated upon, the lesions were classified into three groups: endometriosis of the serosa of the pelvis, endometriosis of the retrocervical region, and endometriosis of the retro-uterine region. Endometriosis of the ovary often developed in all three groups. In the last two groups extraperitoneal foci developed in the rectum, other parts of the bowel, in the dorsal part of the vaginal vault, in the umbilicus, and in the inguinal canal. In early cases the lesion was most commonly localized on the serous surface of the fossa of Douglas. As secondary diseases, uterine fibroids, ovarian tumors, portio carcinoma, and tubal pregnancy were observed.

The disease was observed more commonly in women between the ages of thirty and forty years, although 1 case was observed at the age of fifteen and 2 patients were over fifty years of age. One hundred and forty of the patients were married. The author calls attention to the observation that most of his patients were of an asthenic type with genital infantilism. Most of them lived in cities and gave a history of not having done physical labor.

Dysmenorrhea was the most common symptom; it occurred in 72 per cent of this series and had been present since the menarche in 49 per cent of the patients. Symptoms of peritoneal irritation were observed in 44.5 per cent. Forty-six per cent of the patients had rectal symptoms and 7.2 per cent had

symptoms referable to the urinary bladder. Menorrhagia and metrorrhagia occurred only in advanced cases and were most frequently evoked by secondary diseases. Twenty-eight per cent of the patients had a comparative oligomenorrhea in the early stages; 90 per cent of the married women had either a primary or secondary sterility.

Twenty-two per cent of the patients were treated with a radical operation; 78 per cent were treated with a conservative operation; and the possibility of conception was preserved in 63.5 per cent. Manifest recurrence developed in 6 patients and latent recurrence in 3 patients who had conservative operations. Of the previously sterile married women 31.7 per cent conceived after the operation.

RULON W. RAWSON, M.D.

**Payne, F. L.: The Clinical Aspects of Pelvic Endometriosis.** *Am. J. Obst. & Gynec.*, 1940, 39: 373.

Pelvic endometriosis is characterized by the potential multiplicity of its sites of invasion. The majority of the lesions occur in the ovaries and the cul-de-sac, but any of the pelvic structures or the contiguous viscera may be affected.

It is a disease of middle and late menstrual life, with an incidence of approximately 80 per cent between the fourth and sixth decades. Additional pelvic pathology accompanies endometriosis in four-fifths of the cases to obscure its presence and to cloud the diagnostic picture. The chief symptoms of endometriosis are those of local pain, alterations in the menstrual and reproductive processes, and dysfunction of the contiguous organs. The treatment, which may be that of routine observation, surgical intervention, or irradiation, depends upon the severity of the symptoms, the patient's age, and the removability of the major lesions.

Conservatism, particularly in young patients, with preservation of ovarian and, if possible, menstrual and procreative functions is justified by the results: complete or partial relief of symptoms in from 90 to 95 per cent of the cases; need of further treatment in 8 per cent, and subsequent pregnancies in 9 per cent.

EDWARD L. CORNELL, M.D.

# OBSTETRICS

## PREGNANCY AND ITS COMPLICATIONS

**Mafouz, N. P., and Magdi, I.: Ante-Partum Hemorrhage.** *J. Obst. & Gynaec. Brit. Emp.*, 1939, 46: 941.

This article starts with a historical review, and the treatment of placenta previa as practised from eighty to a hundred years ago is summed up as follows:

If bleeding occurred before delivery the obstetrician was advised to ascertain whether the placenta presented over the os uteri, and, if so, whether the os was wholly or partly covered by it. If the placenta was found to be entirely covering the mouth of the uterus and the cervix was dilated to the size of a half-crown, version was performed. In partial placenta previa the membranes were punctured. If hemorrhage did not cease, the child was turned. In patients in whom the os was found rigid, and the bleeding alarming and not to be restrained by other methods, the vagina was plugged with a silk or cambric handkerchief, or lint steeped in oil, vinegar, or a weak solution of alum.

In the old literature dealing with the treatment of ante-partum hemorrhage, there are several points of outstanding importance, the value of which is as great today as it was when they were first given a hundred years ago. The value of giving blood transfusions before proceeding with the operation if the patient is in poor condition is stressed. The danger of vaginal examinations is emphasized, it being thought that such examinations might initiate serious hemorrhage. A warning against constipation and violent purging is given for the same reason. Rapid extraction after version is interdicted lest the uterus will not contract well after delivery.

The subsequent history of placenta previa brings into prominence four other methods of treatment which, together with rupture of the membranes and application of a binder, have become established in modern times.

*Barnes's hydrostatic dilators.* Barnes's method, as described by him, consisted in dilating the cervix by hydrostatic dilators. These were special bags which he introduced inside the cervix after separating the placenta from the wall of the uterus by sweeping the finger around in a circle.

*Bringing down a foot.* This consists in turning the child by the two-finger method in an early stage of labor, and, after rupture of the membranes, bringing down a foot so that the buttocks of the fetus will press against the placenta. The bleeding sinuses should be tamponed. Further delivery was left to Nature.

*Cesarean section.* The failure of vaginal methods in many cases naturally paved the way to the adoption of abdominal section to meet a condition of undoubted gravity. Despite authoritative opposition from conservative obstetricians, the method has steadily gained in popularity and has spread all over the world. Mackenzie's study of 22,115 cases collected from all over the world indicates the superiority of this method.

*Willett's forceps.* In 1925, J. A. Willett, of London, devised a special forceps for application to the scalp of the fetus, to which weight traction is appended. The compression of the placental site by the head, thus applied, helps to stop bleeding and assists in dilating the cervix.

### RESULTS OF TREATMENT IN PLACENTA PREVIA

In the maternity service of the Kasr El Aini Hospital during the last ten years there were 314 cases of placenta previa among 18,467 deliveries, an incidence of 1.7 per cent. About 0.6 per cent probably represents the true incidence.

The placenta was lateral in 68 patients, marginal in 184, and central in 62; or 21.6, 58.7, and 19.7 per cent, respectively. Thirty-four patients (10.8 per cent) were primiparas, and 280 (89.2 per cent) were multiparas. The average parity was five, and the average age was thirty-two.

Four patients (1.2 per cent) of the group of 314 were pregnant between twenty-four and twenty-eight weeks, 63 (20.1 per cent) between twenty-eight and thirty-two weeks, 133 (42.3 per cent) between thirty-two and thirty-six weeks, 98 (31.2 per cent) between thirty-six and forty weeks, and 16 (5.1 per cent) had hemorrhage at term.

The methods of treatment employed were rupture of the membranes and application of a binder in mild or moderate cases with good pains (46 cases), Dobbin's application of forceps to the scalp in moderate cases with cephalic presentation (78 cases), and bringing down a foot in similar cases with breech presentation, or Braxton Hicks's method in the more severe cases in which more positive pressure was required (165 cases).

Cesarean section was reserved for those cases in which the pregnancy was at or near term, especially when such cases presented themselves with an undilated os and were considered to be free from the chance of infection. Only 12 cases were treated by this method.

Of the 314 patients, 19 died, a gross maternal mortality of 6.1 per cent. Of the children, 154 were still-born, a mortality of 49 per cent. Prematurity was the chief cause of fetal mortality. Marr analyzed 146 cases of placenta previa which occurred among 33,464 deliveries. In 40 of these 146 cases cesarean section was performed, with a mortality of 2.5 per cent, in contrast with a mortality of 5.6 per cent among the cases treated by vaginal methods. The fetal mortality was 20 per cent among the cesarean group and 49 per cent among the vaginal group. Binder reports 84 cases among 9,000 consecutive deliveries. The gross mortality was only 2.4 per

cent. The fetal mortality was 60 per cent. Thompson reports a series of cases in which the mortality of cesarean section was 6 per cent, while 36 patients treated by the insertion of the hydrostatic bag all recovered. Greenhill reports 118 cases of which 42 were treated by abdominal section with no mortality, and 76 by vaginal methods with 4 per cent mortality. Wilson gives a series of 102 cases, of which 32 were treated by cesarean section with no mortality, while 70 treated vaginally had a mortality of 4.3 per cent.

Daily, of the Chicago Lying-in Hospital, reports a series of 139 consecutive cases (1927 to 1934) with no maternal mortality, and with a fetal mortality of 22 per cent.

Cesarean section by the lower uterine-segment technique is the treatment usually favored, and accounts for 58 cases of the series. Of the remaining 81 cases, 25 were treated by rupture of the membranes, 18 by bipolar version, 12 by insertion of the hydrostatic bag, and 6 by Porro's operation.

Of the 4,580 cases analyzed by Berkeley, 1,911 were treated by one of the five principal methods now practiced. Of these 1,911 cases 502 were treated by cesarean section, with 21 deaths; 571 by bipolar version, with 30 deaths; 391 with scalp traction, with 4 deaths; and 391 by rupture of the membranes, with 5 deaths. Fifty-six cases were treated by insertion of the hydrostatic bag. Berkeley is in favor of the use of a single method of treatment as against what he calls composite methods. Cesarean section is advocated as the safest method of delivery in placenta previa for both mother and child, especially in patients with thirty-six weeks of pregnancy or over. The gross maternal mortality of this method is about 4 per cent, and the fetal mortality is around 15 per cent; the maternal mortality of bipolar version is nearly 7 per cent, but the fetal mortality is 85 per cent.

Berkeley gives the following points to be observed in the treatment of patients with placenta previa:

1. Control the bleeding as soon as possible.
2. Do not make a vaginal examination unless prepared to embark at once on an appropriate treatment.
3. Combat the shock, if such is present.
4. Take every precaution to prevent septic infection.
5. Do not hasten delivery, except in cases of cesarean section.
6. Perforate the placenta, if necessary, with a sharp pointed instrument.
7. Whenever possible the patient should be treated in a hospital or first-class nursing home, with expert assistance.

### ACCIDENTAL HEMORRHAGE

In the maternity service of the Kasr El Aini Hospital there were 83 cases of accidental hemorrhage among 18,467 deliveries during the last ten years, an incidence of 0.44 per cent. Of this group of 83 patients 12 were primiparas and 71 were multiparas, a percentage of 14.4 and 85.6, respectively. In 14 cases, or 16.8 per cent, the hemorrhage was of the concealed type.

Of the 83 patients 16 died, a mortality of 19.2 per cent. Of the children, 51 of the 84 were stillborn, 1 patient having twins, a mortality of 60.7 per cent. Most of the mortality occurred among those with the concealed type of hemorrhage.

The average age in the whole group was thirty years, and the average parity was 4.

#### THE ETIOLOGY OF ACCIDENTAL HEMORRHAGE

In spite of extensive work on the subject, the primary cause of separation of the normally implanted placenta remains obscure. Trauma is one cause: in the author's series of 83 cases trauma appeared to be a factor in 5. Trauma, of course, may simply be the exciting factor in a patient on the verge of bleeding.

The association of pre-eclamptic toxemia and eclampsia with placental, retroplacental, and myometrial hemorrhage has been noted by many authors. Albuminuria was present in a large proportion of the author's patients, amounting to 86.7 per cent, and was associated with other signs of toxemia.

It may also be difficult to say whether the toxemia is the cause or the result of the hemorrhage. Thrombosis of the ovarian vein has been suggested as a possible cause.

The renal function is impaired in many cases but returns to normal some months after delivery, which shows that true chronic nephritis is not present. The hypertension observed in some cases is not necessarily from nephritis, but may be due to toxemia.

Bartholomew and Kracke favor the theory of placental infarction in the explanation of the etiology of pregnancy toxemia and placental separation. There is insufficient histological or clinical evidence to support this view.

Couvelaire, Essen-Moller, and others described characteristic lesions in the uterine wall which serve to explain the failure of the organ to contract but still leave us in the dark as to the primary cause of these lesions.

Multiparity is said to be a strong predisposing factor. Only 19.2 per cent of the cases collected by Holmes were those of primiparas. In Williams's group 30 per cent of the patients, and in the authors' group 14.4 per cent, had accidental hemorrhage in their first pregnancy.

Sudden emptying of the uterus, especially in hydramnios and twin pregnancy, severe torsion of the organ, and traction on a short umbilical cord have all been blamed, on mechanical grounds, for accidental hemorrhage.

German writers suggested chronic endometritis as the cause, and brought multiparity forward as a strong argument in favor of their view. Modern conception renders this theory hardly tenable.

Heim found an excess of Prolans A and B in the urine of the toxemic type of patients, and Shute found excess of estrogenic substance in the blood, suggesting an endocrine factor.

Avitaminosis, particularly deficiency of Vitamins E and C, and even allergy were suggested to be causative factors.

THE DIFFERENTIAL DIAGNOSIS OF ANTE-PARTUM HEMORRHAGE

In cases in which the cervix is undilated the differential diagnosis between accidental hemorrhage and lateral placenta previa is always difficult.

Earlier writers laid stress on the recurrent nature of the bleeding and its entirely painless character in placenta previa, and on the pain, distress, and sense of tightness in accidental hemorrhage.

Although albuminuria and hypertension are not invariably present in accidental hemorrhage and may be present in association with placenta previa, they still have a place in the diagnostic assessment of difficult cases of ante-partum hemorrhage.

The demand for early diagnosis in the attempt to reduce the maternal and fetal mortality of such a grave complication of pregnancy has led to the introduction of various aids to clinical methods of diagnosis.

Shute considers that in all cases of accidental hemorrhage there is an excess of estrogenic substance in the blood and a hormone-vitamin imbalance which can be detected by testing the serum of the patient.

The injection of strontium iodide or Uroselectan B into the amniotic sac through the abdominal wall makes it possible to outline the placenta clearly in an x-ray film. The great risk of this method, however, is the liability to bring on premature labor.

Snow, Miller, and Powell showed that it is possible to demonstrate the placenta even in an ordinary x-ray film, but the reading of such films is difficult. Ude, Walter, and Urner have shown that it is possible to diagnose placenta previa by taking an x-ray film after the injection of sodium-iodide solution into the bladder.

The value of these tests remains to be proved by further research. However, the difficulties in making a correct diagnosis in some cases of ante-partum placental separation are still so great that in some cases a correct diagnosis can be made only by careful examination of the placenta after its delivery.

DANIEL G. MORTON, M.D.

**Ince, J. G. H.: On the Value of Cephalometry in the Estimation of Fetal Weight, Based on Measurements of 1,000 Infants.** *J. Obst. & Gynaec. Brit. Emp.*, 1939, 46: 1003.

With the increasing use of the x-rays in obstetrical practice, attention has been directed to the value of intra-uterine cephalometry in the attempt to determine the maturity and the weight of the fetus. The series of cases discussed consists of 1,010 babies delivered at University College Hospital during 1938. All the babies were weighed at birth, and the biparietal and occipitofrontal diameters were measured on the fourth day. This day was chosen in order to allow molding to disappear.

The relation between the biparietal diameter and the birth-weight was worked out, and the equation

$$W = 4.62 \times B - 9.79$$

in which W is the weight in pounds, and B is the biparietal diameter in inches, was formulated. The biparietal diameter is of little value in determining the real weight of a given fetus before birth. It may be used, however, to form a rough estimate of the probable weight.

The biparietal measurement in this series varied from 3.30 to 4.05 in. at term. This variation is too great to allow accurate estimation of maturity in any given fetus. The relation between the biparietal and the occipitofrontal diameters has been worked out in this series and, while there is a definite relation between the two measurements, the range of variation is too great to allow accurate prediction in any given case.

From the observations made on this series of cases the following equation was formulated to calculate the birth-weight from the occipitofrontal diameter:

$$W = 3.98 \times O - 11.23$$

in which W is the weight in pounds and O is the occipitofrontal diameter in inches. This equation gives a correlation coefficient of $0.677 \pm 0.017$. The standard error of prediction is 13½ oz.

The range of values found for any given measurement of the occipitofrontal diameter is here too great to allow an accurate estimate of the weight in any given case. Thus, these measurements can only give a rough guide to the average weight and maturity. The minimal weight to be expected from any given measurement is about 2¼ lb. below the estimated weight; but as the series contains only 28 observations on babies under 5 lb. in weight it cannot be relied on to give the absolute minimal weight.

DANIEL G. MORTON, M.D.

## LABOR AND ITS COMPLICATIONS

**Kepp, R. K.: The Therapeutic Use of Follicle Hormone in Prolonged Pregnancy and in Primary Inertia** (Ueber die therapeutische Anwendung des Follikelhormons bei Uebertragung und bei primaerer Wehenschwaeche). *Geburtsh. u. Frauenheilk.*, 1939, 1: 650.

This article is a detailed consideration of the important work up to the present time on the significance of follicle hormone and other factors in the onset and conduct of labor. In the Universitaets-Frauenklinik at Goettingen follicle hormone was used therapeutically for one year for the induction of labor in prolonged pregnancy and in the management of primary inertia. A trial was first made of a course of quinine and pituitrin. If this failed it was repeated in a few days and supported with follicle hormone. Progynon B ol. forte (50,000 international benzoate units of estradiol-benzoate) in a total dose of from 50,000 to 200,000 international benzoate units was used; later also estradiol (dihydro-follicle hormone) was admin-

istered intravenously in doses of from 5 to 10 mgm. Of 56 cases of probable (not definitely proved) prolonged pregnancy, 27 responded to the first course. In 10 of the remaining 29 patients, it was possible, after further courses with the addition of follicle hormone inserted at various times, to bring about a labor leading to delivery. In 4 of the 10 children the prolonged pregnancy could be definitely established. In 2 cases of intra-uterine death of the child before the onset of labor progynon was given with the first course. In the case of the prolonged pregnancy this combined course was successful; in the second case (a seven months' pregnancy) it was not. One induction of labor by means of progynon at the calculated time of term failed. The result was more definite in cases of true primary inertia. In 15 of 18 instances a definite improvement of the labor contractions was observed about one-half hour after from 50,000 to 100,000 international benzoate units were administered; the uterus which had previously been almost refractory to quinine and pituitrin responded better to their immediate renewed administration. Injuries to the mother and the child were not observed.

(Herrnberger). Richard Warren, M.D.

**Waters, E. G.: Supravesical Extraperitoneal Cesarean Section.** *Am. J. Obst. & Gynec.*, 1940, 39: 423.

Thirty-two patients have been operated upon by the technique described by the author. Twenty-four were primiparas and 6 were multiparas. Of the latter, 3 had previous cesarean sections. There were no maternal deaths and 1 fetal death among the 32 cases.

The operating time for the entire group ranged from twenty-nine to eighty-two minutes and averaged fifty-four minutes. The average stay in the hospital was eighteen days, although half of the patients were discharged within fourteen days after the operation.

The bladder peritoneum is extremely adherent to the perivesical fascia but both as a unit are separable from the bladder. It is then possible to identify the perivesical and periuterine portions of the fascia endopelvina, and by incising them in given manners and planes, permit adequate separation of the bladder from the uterus. Once accomplished, these two maneuvers should permit the bladder to be dropped down and forward from the lower uterine segment, and the separated supravesical peritoneum with attached fascia and the periuterine fascia and peritoneum to be held upward, a large exposure of the lower uterine segment being obtained in this fashion.

In actual dissection of the bladder peritoneum, the subperitoneal tissue is carried away with it, its vitality being thereby conserved and its postoperative reattachment facilitated. If the uterus now be incised transversely, in a crescentic manner with apex downward, several effects are obtained. The curved incision, acting as the "diameter for the circular birth opening in the uterus," is more effective than a straight line between its terminal points could possibly be, for the longer line or diameter allows a larger "birth circle" in the elastic uterus. The technique is fully described.

Edward L. Cornell, M.D.

## PUERPERIUM AND ITS COMPLICATIONS

**Rosenthal, A. H., and Stone, F. M.: Puerperal Infection.** *J. Am. M. Ass.*, 1940, 114: 840.

Two cases of vegetative endocarditis due to the hemolytic streptococcus, Groups B and C, were observed; one was postabortal and the other probably post-partum. Death occurred in both cases. The death due to the Group C streptococcus is believed to be the first of its kind reported. Massive sulfanilamide therapy failed in both cases, although the retention of infected placental tissue may have been a contributory factor in 1 case.

*In vitro* and *in vivo* experiments were carried out to determine the effect of sulfanilamide on the particular strains of streptococci found in these 2 cases. The results indicated little or no chemotherapeutic effect. Charles Baron, M.D.

## NEWBORN

**Clifford, S. H.: Asphyxia of the Fetus and the Newborn Infant.** *Am. J. Obst. & Gynec.*, 1940, 39: 388.

Intra-uterine asphyxia produces fetal damage proportional to the degree and duration of the anoxemia and to the susceptibility of the individual fetus.

A hypothetical explanation of the physiology of asphyxial injury is presented. As the result of asphyxia every organ and tissue of the fetus is subjected to a varying degree of vascular congestion; with further continuation of the asphyxia, every organ and tissue may develop a varying degree of edema, hemorrhage, and cell injury. The resulting clinical manifestations are dependent on the degree and extent of the underlying pathological changes.

The prevention of fetal asphyxia demands methods of obstetrical anesthesia and analgesia that do not produce fetal anoxemia or injure the fetal respiratory center.

The practice of holding the head back and abnormally prolonging the second stage of labor may produce a dangerous degree of fetal asphyxia and should be abolished. Efforts should be made to shorten the second stage when conditions are favorable.

A varying amount of fetal anoxemia is an unavoidable part of certain complications of pregnancy. The ideal method of obstetrical management under these conditions represents individual treatment of each complication. In general, a method of treatment should be sought that will minimize the degree and duration of the intra-uterine asphyxia, yet at the same time safeguard the mother's welfare. In the case of intra-uterine asphyxia resulting from placenta previa a plan of treatment beneficial to both mother and child has been developed.

The prevention of intra-uterine asphyxia or the minimizing of its effects when it is unavoidably present should result in a real reduction in fetal and neonatal morbidity and mortality.

EDWARD L. CORNELL, M.D.

**Fopp, J.: Investigations into the Quantity and Distribution of Liver Glycogen in the Newborn** (Untersuchungen ueber die Menge und Verteilung des Leberglykogens beim Neugeborenen). *Helvet. med. acta*, 1939, 6: 466.

In 24 premature (from seven to nine months) and 56 full-term newborn infants it was determined that the glycogen content of the liver is, in general, high and especially so in the first hour after birth. From the seventh to the ninth fetal month the glycogen content of the liver appears to be somewhat constant, while a few hours after birth, it sharply decreases. In comparison with the liver of non-selected adult material, the newborn liver appears to have a high glycogen content. If, however, the comparison is made with correspondingly active material, i.e., from healthy individuals who have died suddenly, no difference is discernible.

The fetal glycogen, in many cases, shows an extraordinarily high resistance to post-mortem disintegration, in contrast to the usual behavior in the adult. Glycogen granules are never found in the fetus or in the newborn; accordingly there is often a marked post-mortem deposition of glycogen in the lymph spaces, capillaries, central veins, and, less often, in the connective tissue of Glisson's capsule and in the branches of the portal vein. The morphological pattern of glycogen distribution in the liver cell is the same as in the adult. On the other hand, in the newborn a preference for the central lobules is shown by the glycogen accumulation.

Causes of glycogen depletion in the fetus and in the newborn are: prolonged parturition, intra-uterine death a long time before birth, premature separation of the placenta, febrile diseases (lobar pneumonia), and hemorrhagic congestion of the liver. Any influence of the hepatic blood formation or of liver size on glycogen content is questionable, and congenital goiter, thymic hyperplasia, and sex appear to play no rôle. The known antagonism between glycogen and fat deposition can also be demonstrated in the liver of the newborn.

(EFFKEMANN). RONALD R. GREENE, M.D.

## MISCELLANEOUS

**Thoms, H.: The Estimation of Pelvic Capacity.** *Am. J. Surg.*, 1940, 47: 691.

In this monograph, Thoms outlined the methods which may be employed in ascertaining the contours and dimensions of the bony pelvis in the living subject, and pointed out the findings that may be expected from such investigations.

A large proportion of untimely and ill-advised obstetrical operations are the direct result of a lack of proper understanding of the mechanical aspects of labor in which variations in the contours and dimensions of the pelvis may play a major part. The author has studied pelves roentgenologically for nearly a score of years. The useful information obtained has been so impressive that the author recommends the use of roentgen pelvimetry as a routine procedure in primigravidas.

There are two sets of factors in operation in the evolution of the pelvis: (1) developmental and hereditary; and (2) mechanical.

It is of the highest importance that the essential differences between male and female pelves should be thoroughly understood if we are to intelligently study the obstetrical significance of the pelvic capacity.

From the point of view of practical obstetrics there are three portions of the pelvis, the mensuration of which will yield useful information. These are: (1) the plane of the pelvic inlet which includes the anteroposterior, transverse, and posterior sagittal diameters; (2) the midpelvic plane in the lower midpelvis which consists of the anteroposterior, transverse or bispinous, and posterior sagittal diameters; and (3) the planes of the pelvic outlet which include the transverse or bituberal, and posterior sagittal diameters. The above measurements may be considered the cardinal diameters of the pelvis. Of less significance are the diameters known as interspinous, intercristal, external conjugate or Baudelocque, and diagonal conjugate.

The pelvic inlet may assume one of four shapes which may be described as: (1) an anteroposterior oval, dolichopellic or anthropoid type of pelvis in which the transverse is less than the anteroposterior diameter; (2) a circle, mesatipellic or round type of pelvis in which the transverse is equal to, or slightly greater (not more than 1 cm.) than the anteroposterior diameter; (3) a transverse oval, brachypellic or oval pelvis in which the transverse diameter is more than 1 and less than 3 cm. greater than the anteroposterior diameter; and (4) an exaggerated transverse oval, platypellic or flat type pelvis in which the transverse diameter is 3 cm. or more greater than the anteroposterior diameter.

The type of pelvis which for the past two centuries has been considered normal for white women was found in less than 15 per cent of 582 primiparous clinic patients, and in only 6 per cent of 100 young women from a much more privileged economic group. It was, therefore, neither the normal pelvis in the sense of being the most frequently occurring type, nor was it the most adequate type, as gauged by the relative frequency of operative intervention required during labor by the women who possessed it.

It has long been known that marked anteroposterior flattening of the adult pelvis may result from severe rickets during early life. The high incidence of round and of anteroposteriorly elongated pelves among the 100 student nurses suggests the possibility that adequate nutrition during early life and other factors which make for the attainment of

maximum normal body size prevent that degree of anteroposterior flattening of the pelvis which has come to be considered as the characteristic feminine type.

In evaluating the clinical relationship to the types of pelves, the author is convinced that the most favorable type of inlet is that which is round or is elongated anteroposteriorly (mesatipellic or dolichopellic), and not the oval (brachypellic) or "textbook" type of pelvis.

The type of pelvic inlet can be determined in the intact living women only by roentgenographic means. An unsuspected midplane or an outlet contraction may be present at term in the primigravid patient with adequate inlet capacity, in whom the fetal head is engaged, and there is no way of accurately determining such occurrence without roentgen means. Furthermore, the occurrence of wide variations of pelvic form in presumably normally formed individuals is definitely a matter of concern to the obstetrician, and these variations can be established only by means of roentgen investigation. CHARLES BARON, M.D.

**Campbell, R. E., and Sevringhaus, E. L.: The Management and Treatment of Habitual Abortion.** *Am. J. Obst. & Gynec.*, 1940, 39: 573.

There were 13 cases in the series. Each patient had aborted twice or more and did not have a living baby. The exception was 1 patient who had a mature living baby followed by 2 spontaneous abortions. Of the 13 patients treated, 11 went to term and had spontaneous deliveries. One patient aborted after four months and the other after six months of pregnancy.

This selected series permits little doubt as to the value of progesterone (2 rabbit units weekly) and corpus-luteum extracts in the treatment of habitual spontaneous abortion. This treatment should not substitute for thyroid deficiencies and other obvious factors which may be responsible for the repeated spontaneous abortions. EDWARD L. CORNELL, M.D.

# GENITO-URINARY SURGERY

## ADRENAL, KIDNEY, AND URETER

**Belgrano, V.: Experimental Studies on the Pathological Anatomy and Function of the Kidney Exposed to Temporary Ischemia** (Contributo allo studio anatomo-patologico e funzionale del rene sottoposto ad ischemia temporanea. Ricerche sperimentali). *Arch. ital. di urol.*, 1939, 16: 435.

The author first reviews the literature, and after a detailed report on the work of numerous authors in this field notes that there have been comparatively few studies of renal function after temporary ischemia of the kidney. Ferrarini and Fulle reported a transitory albuminuria. Hubner noted an increase in the residual nitrogen and retention of water.

The author conducted a series of experiments on rabbits and dogs in which he temporarily interrupted the renal circulation with ligation or forceps for one, one and one-half, and two hours. The renal function was studied in each instance and histological studies were carried out on the kidneys. Detailed tabulations of the structural and functional results in each animal are presented, as well as photomicrographs and roentgenographs.

The following conclusions were drawn:

With a two-hour ischemia in rabbits there was noted sclerosis of the renal parenchyma and epithelial degeneration, most extensive in the renal cortex. Deposits of calcium salts sufficient to show up in the x-ray film were also observed. In some of the kidneys from this group the structural changes were mild and the glomeruli and vessels were not involved. In dogs, after a two-hour ischemia of the kidney, foci of sclerosis and epithelial degeneration were observed in the renal cortex alternating with apparently normal areas. With a one-and-one-half-hour ischemia the lesions in the kidney were more circumscribed and less serious, with a predominance of normal renal tissue. With only a one-hour ischemia no noteworthy lesions were observed in the kidney. The author's findings agree with those of Litten, Israel, Werra, and Jatta, who found serious renal lesions only after two hours of ischemia. The function of the kidney was found to be well preserved after two hours of ischemia. The author found that in 50 per cent of the rabbits and in 3 of 4 dogs the renal function was normal according to intravenous pyelography. A mild and temporary albuminuria was noted in some instances. There was no difference noted in the renal reactions of dogs or rabbits to the ischemia, except for a more abundant precipitation of calcium salts in the rabbit. JACOB E. KLEIN, M.D.

**Oppenheimer, G. D.: Evaluation of Roentgenography of the Surgically Exposed Kidney in the Treatment of Renal Calculi.** *J. Urol.*, 1940, 43: 253.

The incidence of recurrence after conservative operation for renal calculi varies between 4.6 and 60 per cent in various clinics, because of such factors as differences in the follow-up time, accuracy of the observations, and the type of cases treated.

Of 422 cases of calculous disease of the upper urinary tract observed at Mt. Sinai Hospital, New York City, between the years 1928 and 1933, 85 per cent were followed up for an average period of four years. Twelve and one-tenth per cent of the patients were nephrectomized, 40 per cent underwent conservative renal surgery, and 17.3 per cent, ureterolithotomy. Conservation of the renal tissue was the guiding consideration. Of 130 patients operated upon for unilateral calculous disease, 14.6 per cent had subsequent calculus formation on the opposite side after the original observation of unilateral disease. The operative results in 141 cases of all types—aseptic, infected, unilateral, bilateral, primary, and secondary stones—showed that the true recurrence rates for pyelolithotomy, pyelonephrolithotomy, nephrolithotomy, and the total rate for all the operations were: 14.9, 32, 29.4, and 21.1 per cent respectively; the residual recurrence rates were 10.6, 32.4, 41.4, and 22.7 per cent, respectively; and the totals of the true recurrence and residual recurrence rates were 24, 54, 58.6, and 39 per cent, respectively. The presence of residual calculi, or their absence was determined by routine control roentgenography at the time of the patient's discharge from the hospital. The total incidence of recurrence after operation would be materially reduced if the problem of residual recurrence were completely solved. In the meantime, the frequency of true recurrence may possibly be reduced by the control of infection with the newer chemotherapy (sulfanilamide, azosulfamide, mandelic acid), high vitamin diets, or by resection of persistent infected and deformed portions of calculous kidneys.

The use of kidney x-ray control at the time of operation to help find stones which are impalpable or which have been overlooked takes care of the residual-calculus situation. The technique follows:

All the stones or fragments that can be located are removed from the kidney pelvis and calyces. The previously mobilized kidney has a necktie packing placed around it in sling fashion for traction. A Buck kidney film, measuring 3¼ by 3¼ in., which is encased on one side by tinfoil and on the other side by black paper, is placed in a thin sterile rubber bag. The bag with the black paper side forward is placed deeply into the wound against the posterior aspect of the kidney, the latter being raised by the gauze sling. Three or more needles are then inserted into the convex border of the kidney as markers. For purposes of identification the one to the lower pole has its eye down as contrasted with the points down of the other needles. All retractors and artery clamps are removed. Using a Waite-Bartlett shockproof bedside x-ray unit, with a 5 in. gap, 30 ma., and with

the tube at about a distance of 36 in. from the film, an exposure of about 3 seconds is made. The bag with the film is then removed and the developed film is shown to the surgeon in about four minutes. Any remaining stones or fragments shown on the film are then removed. If the kidney cannot be mobilized, a large film may be placed behind the kidney and the general kidney region exposed to the x-rays. The outline of the kidney is indicated by means of a bent probe placed around the periphery for this purpose. The real advantage of the control x-ray procedure was demonstrated by the fact that stones were found and removed from 15 of 33 patients in whom stones or fragments were not palpable or found without roentgenograms.

During the last five years, 52 patients were subjected to x-ray control while being treated surgically for multiple or dendritic calculi. The total for the ten-year period was 85 of such examinations. In 29 patients, stones or fragments which were impalpable, or found without the aid of roentgenograms, were located by x-rays and removed. In 17 patients stones were seen but could not be removed, in some cases because of the patient's general condition. In other cases only some of the stones or fragments could be removed. In 55 of a total of 63 cases in which the x-ray control indicated the absence of residual concrements, this indication proved to be correct. In 2 patients calcific shadows were seen but there were no calculi. In several patients the operative x-ray control was negative, but small concretions were removed in spite of the negative finding on the film. In cases of movable calculi, this technique is also of value in finding a small stone, especially one that cannot be palpated. In secondary operations, or in cases of patients with a small extrarenal pelvis, roentgenography may be helpful and particularly useful in preventing much trauma incident to extensive exploration for an elusive stone. Localization is also valuable in finding a stone hidden in a calyx in the presence of hydronephrosis, or behind a strictured neck of a calyx.

LOUIS NEUWELT, M.D.

**Podio, G.: The Value of Roentgen Therapy for the Suppression of the Function of the Kidney in Ureteral Lesions** (Sul valore del trattamento roentgenterapico per la soppressione della funzione del rene in casi di lesioni ureterali). *Riv. ital. di ginec.*, 1939, 23: 77.

A patient was presented with a ureteral fistula which had developed following complete hysterectomy. In accordance with the proposal of Klein, the author tried to suppress the function of the kidney on that side by roentgen irradiation. After an unsuccessful trial of six months' duration, a nephrectomy was done, with removal of a large pyonephrotic kidney. A careful study of the literature on this procedure was then made.

It is believed that many factors may influence the result. Among them are age, obesity, the original gynecological malady, the time elapsing between the operation and the appearance of the fistula and the beginning of the irradiation, and the condition of the urinary system before operation. One should keep in mind the action of the rays, not only upon the kidney but also upon the fistula proper and the surrounding tissues. During the treatment, careful periodic examinations of the urinary system should be made in order to anticipate any complications. These examinations are also of value in determining the exact mechanism responsible for cessation of leakage through the fistula, if it should occur. This cessation may be associated with closure of the fistula with patency of the ureter and conservation of renal function, with blockage of the ureteral stump and consequent atrophy of the renal parenchyma, or with true cessation of renal function secondary to irradiation.

When the condition of the patient and the technical difficulties preclude operation for the fistula, the method of Klein should be tried. This set of circumstances is apt to occur particularly following the Wertheim operation. FRANK MCDOWELL, M.D.

## BLADDER, URETHRA, AND PENIS

**Di Giacomo, A., and Berti Riboli, E.: Enlargement of the Bladder Capacity by Means of an Intestinal Loop** (Contributo allo studio dell'ampliamento della vescica con ansa intestinale). *Arch. ital. di urol.*, 1939, 16: 406.

The urologist has occasion to treat patients whose bladders have lost their normal capacity and when a few cubic centimeters of urine are expelled they experience much pain and tenesmus. This condition may be due to chronic inflammation or ulceration of the bladder with resultant hyperexcitability of the musculature of the bladder. Careful differentiation should be made between functional and organic disturbance of the bladder function. With chronic inflammation all the structures of the bladder wall may be involved and lead to scar formation and shrinkage. The most common causes of diminished bladder capacity are ulcers of the mucosa, embolus, thrombosis, and spastic contraction of the capillaries, which lead to disturbance of nutrition of the mucosa with resultant ulcer formation. In such cases there is frequently an associated reflux into the ureter and renal pelvis. Cystoscopy reveals an atrophic, yellowish, pale mucosa; avascular and, at times, scar formations may be noted. The treatment for this condition is a vesico-enteral plastic operation.

The success of such a procedure depends on three factors: the choice of the proper indications and time for intervention; a precise knowlege of the mechanism of the function of the bladder; and a knowledge of the operative technique involved. Before intervention it is necessary to reduce the local inflammation and the condition of the urine by proper local medication of the bladder. The author then discusses in detail the physiology of the bladder and points out that the fundus of the bladder is very mobile and is always in contact with intestinal loops.

The literature on the operative technique is reviewed from 1899 to 1939. The authors note the possibilities of such complications as ascending pyelonephritis. They believe that there is least danger of ascending infection when a loop of small intestine is used for the plastic operation. They describe and illustrate by drawings the various types of operations suggested by Scheele, Rubritius, Strassmann and Birnbaum. After a loop of small intestine has been isolated for this purpose the mucosa is washed with oxycyanate of mercury 1-1000 to avoid the possibility of infection. This mucosa after implantation becomes atrophic; there is no absorption of urinary excretion products from the intestinal mucosa.

The authors review the literature on the experimental operative technique and note that animal experimentation in this field was first performed by Tizzoni and Foggi of Bologna in 1888. The authors' personal experiments were done on a series of 10 female dogs under general anesthesia. After the bladder had been walled off by sponges from the general peritoneal cavity a loop of small intestine was isolated, while the rest of the intestine was reunited by a lateral anastomosis. The new plastic wall was attached by silk sutures to the fundus of the bladder, which the author considers the most favorable site for the new addition to the bladder wall. The dogs were kept on a liquid diet for ten days after surgery. Bloody urine was emitted for the first twenty-four hours after operation. Of the 10 animals operated upon, 1 died of peritonitis on the third day after operation; another dog died on the fifth day after surgery from an ascending pyelonephritis. The authors present detailed protocols of the dogs which were operated upon and x-ray studies of the completed bladders.

The authors conclude that anastomosis of the bladder with the intestine for the purpose of increasing the capacity of the former leads to successful anatomical and functional results. The success in dogs leads to the conclusion that the same technique may be successfully used in man, although the procedure in man would be more difficult because it is not easy to exteriorize the bladder in man. The authors found that the transverse position of the plastic loop of small intestine when attached to the bladder fundus is the most practical.

JACOB E. KLEIN, M.D.

**Goin, L. S., and Hoffman, E. F.: A New Approach to the Treatment of Certain Bladder Carcinomas.** *Radiology*, 1940, 34: 205.

A summary of the indications and methods for the treatment of carcinoma of the bladder are reviewed by the authors. It is their opinion that since 75 per cent of all tumors of the bladder involve either the trigone or the neck of this organ, or both, and a large percentage are either so far advanced or so extensively infiltrated when they are first seen, they do not lend themselves well to modern procedures. For this group of tumors, or selected instances in this group, the authors propose marsupialization of the bladder and intense radiation *in situ* by the contact therapy method. On the ninth or tenth postoperative day contact therapy is begun and treatment given on alternate days until a total dose as high as 303672 roentgens is given over a period of twenty-seven days.

No untoward results were observed in a series of 3 cases presented and the authors believe that in selected cases a great deal more can be offered to a patient with carcinoma of the bladder by the use of this combined surgical and radiological method than by either fulguration or cystectomy.

D. E. MURRAY, M.D.

**Tempesta, F.: Urethral Calculus** (Sulla calcolosi uretrale). *Ann. ital. di chir.*, 1940, 19: 131.

The author reports the case of a forty-five-year-old man with complete acute urinary retention. The patient had never had renal colic. At the age of thirty he had acquired gonorrhea, which was cured after one year. This was followed by stricture, which required internal urethrotomy and occasional dilatation. At various times there had been recurrences of symptoms, such as strong pains during micturition, interruption of the urinary stream, mild hemorrhage, and a small tumefaction on the ventral surface of the penis near the scrotum. Urethral catheterization demonstrated an obstruction several centimeters from the meatus. With difficulty a soft catheter was passed into the bladder; the urine was found to be turbid and alkaline and contained a sediment rich in ammonium-magnesium phosphate. X-ray examination demonstrated two urethral calculi, one proximal and conicocylindrical in shape, and the other irregularly pyramidal in form. These were probably two fragments derived from one original calculus. Because of the stricture, removal of the calculi per vias naturales was out of the question. An external urethrotomy was done at the level of the stricture and two phosphate stones were removed. Exploration with a sound higher up toward the bladder revealed no other stones. The urethra was sutured over a semi-rigid catheter. The patient was cured and left the clinic after twenty days of hospitalization.

The author notes that this case is interesting because of the great rarity of urethral calculus and because of the large size of the calculi here. The male urethra because of its tortuosity, irregularity of caliber and stenoses both congenital and acquired is a suitable site for calculi. As to origin, these calculi may be either migratory or autochthonus. The former arise in the upper portions of the urogenital tract, and are stopped at constricted areas whether natural or acquired. The autochthonus type is most rare and the calculi are formed locally in areas of inflammation, stricture, and diverticulum. These are usually mixed calculi and attain large dimensions, as in diverticula. The mucous and fibrinous exudates form the nucleus for the deposition of carbonates and phosphates of calcium and ammonium-mag-

nesium phosphate. Frequently the nuclei are formed by foreign bodies or bacteria. Hellström has observed 90 cases of urinary lithiasis caused by the staphylococcus.

In the author's patient the calculus was autochthonus and due to stricture. The symptoms of such cases are varied and usually include dysuria, interference with the urinary stream, and urethrorrhagia. The diagnosis is easy when pain is followed by urinary retention. Palpation discloses a large calculus of the penile urethra. Catheterization helps diagnosis by showing arrest of the sound by a hard object. It also aids in determining the site of the calculus. Roentgenography and urethrography finally clinch the diagnosis. The treatment depends on the location and size of the calculus, as well as the condition of the urethra. Small stones may be passed naturally. If not far from the meatus they may be grasped by suitable forceps and withdrawn. When the latter procedure is impossible external urethrotomy is indicated. In difficult cases a cystotomy and even a prostatectomy may have to be done to remove a large calculus. There is a tendency toward recurrence of urethral calculi; for this reason it is preferable, when possible, to do an external urethrotomy so that a local stricture may be cured and all fragments of calculi cleaned out. JACOB E. KLEIN, M.D.

**Mallone, T.: Calculus of the Urethra** (La calcolosi dell'uretra). *Ann. ital. di chir.*, 1940, 19: 109.

The author reports an unusual case of stone in the urethra and presents a thorough review of the literature on this subject. He notes that stone in the urethra is a very rare condition in urological practice. Burckhardt gives the incidence as 0.10 per cent and Britneu as 0.82 per cent. Usually it occurs in males and affects individuals in the first decade of life. The infantile state of the prostate at this period permits the passage of large stones into the urethra. The calculus may be a primary formation in the urethra or may be secondary to formations higher up in the urogenital tract. In most of the cases there is a local stenosis with scarring, inflammation, and dilatation with urinary retention and sepsis. The characteristic site is the membranous urethra. In a series of 36 cases reported by Englisch the following localization is noted: fossa navicularis, 11 per cent; penile urethra, 15 per cent; penoscrotal angle, 14 per cent; bulbar urethra, 19 per cent; and membranous and prostatic urethra, 41 per cent. A common predisposing cause is urethral diverticulum with urinary stasis followed by infection and ammoniacal decomposition of the urine. The symptoms vary according to the mode of onset. If sudden, there is acute pain with cessation of the urinary stream through the urethra, and also hemorrhage. Tenesmus of the urinary bladder and an associated urethrocystitis may also develop, or painful erections with pain at the time of ejaculation may be noted. Such symptoms lead to completion of the examination and diagnosis by use of urethral sounds, the urethroscope, and x-ray studies.

The prognosis is reserved and depends on the nature of the complications usually associated. Infection is the rule. There may be an ascending ureteropyelonephritis which may have a fatal termination through renal insufficiency.

The treatment is based on the conditions found in the individual patient. If the stone is in the prostatic part of the urethra it may be pushed back into the bladder by means of a sound and then removed by cystotomy or by lithotrity. If the stone has already passed through this part of the urethra it may pass spontaneously or may be grasped with forceps through the urethroscope. If such conservative treatment is unsuccessful, surgery is indicated. According to the location of the stone, either a cystotomy or an external urethrotomy is done. Even in the latter procedure some authors advise cystotomy for drainage of the infection.

Case Report. A seventeen-year-old boy complained of symptoms of urinary disturbance. These symptoms were chronic in duration, having begun at the age of two years, when a cystotomy was done for urinary retention because of a stone in the bladder. Since then he had suffered at intervals from urinary distress, i.e., from polyuria, nocturia, and even hematuria. For the past three years he had noted a swelling at the root of the penis near the scrotum. He masturbated at times and noted that ejaculation was particularly painful. At the present time the general condition is essentially normal. Locally a hard, nut-like swelling was noted at the under surface of the penis near the scrotal junction. There was a fetid, seropurulent secretion from the urethral meatus. X-ray examination revealed multiple calculi which occupied a large part of the urethra and the prostatic-membranous portion. Urethrocystography demonstrated a considerable dilatation at the site of the pathology. The diagnosis was calculus of the urethra with chronic urethrocystitis. A cystotomy was done but the stone could not be delivered from above. An incision was made below in the median raphe and many stones were extracted. A drainage tube was inserted below and vesical lavage was done daily with permanganate. Subsequently the patient was completely cured after excision of the fistulous tract in the perineum under local anesthesia. Twenty-three calculi were extracted, varying in size from a nut to a seed. The entire collection weighed 62 gm.

There are photographs of the local condition and the stones removed at operation, and the histology of the excised portion of the urethra together with a bibliography is given. JACOB E. KLEIN, M.D.

## GENITAL ORGANS

**Lowsley, O. S.: Total Perineal Prostatectomy.** *J. Urol.*, 1940, 43: 275.

The author reports his modification of perineal prostatectomy as advocated by Young, believing that there is some improvement in the rapidity of healing, with the possibility of reduction of the incontinence.

Some type of regional anesthesia is used and the patient is placed in an exaggerated lithotomy position. The incision is made about 1 in. above the rectum and is deepened through the subcutaneous tissue until the central tendon is exposed. The fossa on each side of the central tendon is explored by blunt dissection, care being taken to avoid dissection too far laterally as the pudic nerve and vessels are liable to injury. The central tendon is incised behind the transversus perinei muscles, which are retracted forward. The dissection is carried above the rectal wall until the apex of the prostate is encountered and the recto-urethralis muscle found. It is incised or pulled over to one side, in order to expose the surface of the prostate, which is recognized by its glistening fascia of Denonvillier.

Further exposure is obtained by separating the fibers of the levator ani until the fascia covering the seminal vesicles is seen. The posterior retractor is now placed in position. The prostate is excised from the membranous urethra, and the gland carefully mobilized, care being taken to leave the supraprostatic fascia. The prostate is now removed from the vesical orifice and, in cases of cancer, the seminal vesicles and ampullæ of the vasa deferentia are also removed. Bleeding points are clamped and ligated.

The repair is accomplished by passing a ribbon-gut suture through the wall of the urethra; this is carried to the inside of the vesical orifice, over behind the apex of the trigonum vesicæ into the bladder lumen again, and then to the outside of the urethral wall. The two ends are then tightly tied. This one suture acts as a hemostatic agent for all the cut edges; it approximates the vesical lumen to that of the urethra over a catheter; it plicates the urethra, thereby reducing incontinence to a minimum. It also eliminates the necessity for packing or a bag. Drainage is maintained through a small urethral catheter. A Penrose drain is left in the wound for twenty-four hours.

This operation is indicated in early cancer, chronic pyemia, intractable chronic fibrosis, calculosis, and in certain cases of tuberculosis and of adenoma of the prostate. ELMER HESS, M.D.

# SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

## CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

**Dunkmann, G.: Osteomyelitis and Its Prognosis** (Die Osteomyelitis und ihre Prognose). *Ergebn. d. Chir. u. Orthop.*, 1939, 32: 527.

This is an extensive study of the international literature on osteomyelitis and a review of material consisting of 314 cases of this disease from the author's own clinic. The author points out the regional difference in the course and severity of this disease. The number of purely traumatic cases is minimal. According to Walter the trauma must have been very severe, the localization of the disease must coincide with the site of trauma, and the osteomyelitis must follow shortly after, if the condition is to be considered of traumatic origin. The great number of methods of treatment—vaccine therapy, hemotherapy, iontophoresis, chemotropic therapy with electrocuprol or salvarsan, maggot therapy, periarterial sympathectomy, Orr's treatment, and the treatment of Payr and Loehr—are discarded. Following the use of the latter methods, which include fixation after opening, unguentolan tamponade and primary closure, removal of the sequestrum after three or four weeks, and renewed unguentolan tamponade and primary suture and fixation, the author saw repeated extensive phlegmons of the soft tissues and erysipelas, which he believes were due to primary suture. He believes the subperiosteal resection is of considerable value.

The author emphasizes the importance of evaluation of the result after complete healing. In the reexamination appalling results are frequently seen. In 133 re-examinations only 2 patients (who had had amputations) could be considered as completely healed. In 2 others a cure was highly probable. In all of the others there was a long-drawn-out illness interrupted by normal periods. In 1 case the interval lasted forty years. The mortality was 12.42 per cent.

The treatment of the acute cases was the multiple drill-hole method of Payr. If pus was present the bony bridges between the drill holes were removed with a chisel, the cavity was filled with unguentolan, and a few tension sutures were applied.

(Lenkeit). Leo A. Juhnke, M.D.

**Lindblom, K.: On the Pathogenesis of Ruptures of the Tendon Aponeurosis of the Shoulder Joint.** *Acta radiol.*, 1939, 20: 563.

The author investigated the tendon aponeurosis after rupture for changes in: (1) the anatomical structure, (2) the vascular system, and (3) the tensile strength. Clinical material was investigated for facts which might throw light on the pathogenic aspects.

Study of the clinical and anatomical material revealed:

1. Rupture of the tendon aponeurosis of the shoulder joint required more than one causative factor.

2. A rupture did not occur in an individual under thirty years of age.

3. Pathologically there was primarily sclerosis of the tendinous tissue.

4. There were no indications that rupture of the tendon aponeurosis was due to wear.

5. There was no relationship between the age of the patient and the size of the rupture.

6. A study of vascular changes in the tendon aponeurosis gave no unanimous conclusions.

7. Histological findings of degeneration in the tendinous tissue could not be proved as being primary to the rupture.

From a study of the clinical material it appeared that primary trauma was an almost constant etiological factor.

Experiments in ruptures of the supraspinatus tendon aponeurosis demonstrated that injury took place with the arm abducted or externally rotated. Therefore ruptures of the subscapularis tendon aponeurosis should require internal rotation of the arm. Experimental investigations showed that rupture of the tendon aponeuroses often took place in stages.

Richard J. Bennett, Jr., M.D.

**Lindblom, K.: Arthrography and Roentgenography in Ruptures of the Tendons of the Shoulder Joint.** *Acta radiol.*, 1939, 20: 548.

The use of arthrography or bursography in the diagnosis of injuries to tendons of the shoulder was suggested by Codman, but he himself was unable to reach any demonstrable conclusions.

Instead of using the terms supraspinatus, infraspinatus, and subscapularis ruptures, the writer refers to ruptures in the respective part of the tendon aponeurosis of the shoulder joint. By the tendon aponeurosis is meant the continuous mass of fibrous tissue formed by the tendons of the short rotators and abductors of the shoulder and the coracohumeral ligament.

The material consists of 54 clinical cases of arthrographically diagnosed ruptures in the tendon aponeurosis of the shoulder joint or in the long biceps tendon; 50 clinical cases, examined arthrographically and found to have no rupture of the tendon aponeurosis or of the long biceps tendon; 3 clinical cases examined bursographically, in which no rupture could be demonstrated, and 38 anatomical specimens, dissected, roentgenographed, and in the majority of cases examined arthrographically and histologically.

*Arthrographical technique.* The patient lies on his back with his arm adducted and relaxed. A hypodermic needle 1 mm. in diameter and with a short bevel is inserted about 1 cm. anterior and lateral to

the acromioclavicular joint in the direction of the center of the head of the humerus. When the point of the needle is in the cartilage of the humeral head, the needle is withdrawn about 1 mm. and the contrast medium, 6 c.cm. of 35 per cent perabrodil mixed with 1 c.cm. of novocaine, is injected into the joint. The roentgenograms are taken without delay, since the contrast medium is absorbed rapidly.

The roentgen technique was done on Lysholm's skull table. Three positions were used in order to provide tangential views of the insertions of the tendon aponeurosis. In exceptional cases a fourth position was added, which gave a picture of the joint as seen from the glenoid cavity. These four positions are very well illustrated in detail in the article.

In the normal arthrogram the contrast medium fills the joint cavity, the tendon sheath of the biceps, and the subscapularis recess. The subacromial, subdeltoid, and subcoracoid bursæ do not under normal conditions become filled from the joint. The appearance of the arthrogram in the various positions is described in detail. Technical errors which may complicate the interpretation of the arthrograms are discussed.

In general, ruptures of the tendon aponeurosis of the shoulder were situated near the greater or lesser tubercle and appeared to have begun in the part of the tendon tissue lying nearest the head. A rupture of the articular parts of the aponeurosis always included the capsule, and a continued rupture including the superficial parts of the aponeurosis always extended to the wall of the bursa. Regarding the arthrographic appearance and the operability, it was found advisable to divide the ruptures of the supraspinatus and infraspinatus portions of the aponeurosis into four groups. Cases belonging to the first two groups were practically the only ones suited for operation.

The ruptures of the subscapularis portion, as in the supraspinatus and infraspinatus portions, were located near the insertion. The diagnosis of this condition by arthrograms is discussed and well illustrated.

In only 1 case rupture of the long biceps tendon was confined to the tendon. In 2 cases there was also a rupture of the subscapularis portion of the aponeurosis. The remaining cases showed lesions of the supraspinatus and infraspinatus portions.

Other roentgenological changes in ruptures of the tendon aponeurosis are discussed and illustrated in detail. Comparison with the cases without rupture in the aponeurosis showed that the only pathognomonic sign of a tendon rupture was the attrition of the greater tubercle and the inferior surface of the acromion, combined with an upward subluxation of the head.

In this material none of the clinical signs, as described by Codman and others, proved to be pathognomonic. On the other hand, the arthrography of the shoulder has possibilities of becoming an infallible method of detecting ruptures in the tendon aponeurosis of the shoulder joint and in the long biceps tendon. The same accuracy in the diagnosis of these ruptures cannot be reached by means of clinical methods, and ordinary roentgen examination of the shoulder is of insignificant value in these cases. RICHARD J. BENNETT, JR., M.D.

**Piergrossi, A.: Lesions of the Femoral Neck in Infantile Osteochondritis of the Hip** (Sulle lesioni del collo femorale nella osteocondrite infantile dell' anca). *Radiol. med.*, 1940, 27: 81.

Piergrossi recalls that infantile osteochondritis of the hip is generally accepted as being essentially a lesion of the femoral epiphysis, but points out that nearly always there are also lesions in the acetabulum and in the neck of the femur. An enlargement of the articular interline appears early and when the epiphyseal lesions are further advanced the acetabulum presents an oval form. In the femoral neck, the lesions may be early or late. The early lesions involve principally the metaphysis, or the portion of the neck immediately below the conjugation cartilage, and may present the following roentgen aspects: (1) more or less irregular foci of decreased density with indistinct borders, and which may or may not be circumscribed by opaque rings; (2) foci of cystic aspect with clearly marked and regular borders, which also may or may not be circumscribed by opaque rings; (3) irregular areas of increased opacity; and (4) marked increase of transparency involving the entire upper extremity of the femur and even extending beyond it to the homolateral part of the pelvis. The late lesions begin during the evolutionary phase and cause irreversible changes in the bone; they include changes in the thickness, the length, and the direction of the femoral neck. The first involve especially the part nearest to the cephalic nucleus and impart a gibbose aspect to the supero-external contour of the neck; the second generally produce marked shortening of the neck which may disappear completely; the third result in coxa vara, including the beret form of coxa plana, or coxa valga, antetorsion, retrotorsion, version, or flexion.

In general, it may be stated that a large number of cases of osteochondritis present lesions of the neck and particularly of the metaphysis which establish themselves during the period of evolution of the disease; they consist primarily of irregular foci of bone rarefaction or, more frequently, of a typical semi-oval, metaphyseal focus. These foci of rarefaction must be accepted as having great importance in the picture of osteochondritis, as they represent probably the primary metaphyseal process from which result part or all of the other changes in the neck. In fact, the metaphyseal foci constitute a process similar to that developing at the same time in the cephalic nucleus, but of lesser gravity and duration. This confirms the concept of Bertolotti that in osteochondritis of the hip there are combined epiphyseal and metaphyseal lesions, or that osteochondritis is especially a meta-epiphysitis. The

lesions found in the metaphysis are not secondary to those of the epiphysis, as claimed by many authors; both run parallel and are due to the same primary cause. In addition, in some individual cases there may be infectious metaphyseal foci which are correlated with but not directly caused by the meta-epiphysitis. As a result of the metaphysitis, other phenomena arise, consisting of cystic formations, zones of osseous condensation, and diffuse osseous atrophy; the periosteal reaction in the neck and the lesion of the conjugation cartilage cause real thickening and shortening of the neck with changes in the orientation of the neck and head.

The described metaphysitis may also occur alone without lesions of the cephalic nucleus, but then it assumes the roentgen aspect of Bertolotti's upper femoral metaphysitis, called by others "infantile coxa vara" or, erroneously, "congenital coxa vara." Although this morbid form is distinct from meta-epiphysitis for many reasons, the two diseases have nevertheless a basic pathogenetic and anatomical identity which requires their inclusion in a larger entity, osteochondritis of the hip. This term consequently means a meta-epiphyseal dystrophy of growth localized solely in the metaphysis (metaphysitis of Bertolotti) and leading to the formation of coxa vara, or in the epiphysis and the metaphysis at the same time (meta-epiphysitis or disease of Calvé-Legg-Perthes-Waldenström) and leading to the formation of coxa plana.

RICHARD KEMEL, M.D.

## SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

**Young, F.: The Use of Autogenous Rib-Cartilage Grafts to Repair Surface Defects in Dog Joints.** *Surgery*, 1940, 7: 254.

In a series of dogs, grafts of rib cartilage were transplanted into surgical defects made in the cartilage of non-weight-bearing areas between the femoral condyles. The defects were made down to the subchondral bone. When the graft was accurately approximated, it healed in place with fibrous-tissue connections and remained viable for at least one year. There was, however, fibrous union of rib cartilage and articular cartilage. When several rib-cartilage grafts were placed in parallel strips on the denuded surface of the knee joint, it was found that these healed to each other by cartilaginous union, but the grafts united to the articular cartilage with fibrous tissue. CHESTER C. GUY, M.D.

**Guibal, A., and Ginestié, J.: Can the Condemnation of the Chopart Disarticulation Be Revised? Anterior Tenosuspension Complementing the Calcaneus** (Peut-on réviser la condamnation de la désarticulation de Chopart? Téno-suspension antérieure complémentaire du calcanéum). *Rev. de chir.*, Par., 1939, 58: 673.

The midtarsal disarticulation of Chopart has been condemned by a great many surgeons over a long period of time. This condemnation has been apparently well deserved because of the very poor functional results which have followed this type of disarticulation.

The anatomical longitudinal arch of the foot is supported by the anterior and posterior extremities of that arch which is made up primarily of metatarsal bones and ligaments. The apex of this arch is the site of the midtarsal amputation of Chopart. The medial portion of the longitudinal arch is supported posteriorly by the calcaneus and anteriorly at the metatarsophalangeal articulation. This bony longitudinal arch is supported also by several important ligaments.

The movements of the ankle at the tibiotarsal articulation are produced by the action of two antagonistic groups of muscles, the anterior group and the posterior group. The greatest disability occasioned by Chopart's disarticulation is the inversion of the stump because after Chopart's disarticulation there is no longer any support on the posterior tuberosity of the calcaneus. When inversion of the foot has once set in following Chopart's disarticulation correction is very difficult.

Methods to prevent the inversion of the foot following the disarticulation may be classified under: (1) prosthesis; (2) orthopedics; and (3) operation. Not any one of the three methods is sufficient in itself, as it requires the combination of all three to obtain good end-results.

1. Prostheses. It is suggested that a solid anterior support is necessary and that the bottom of the shoe should be supported by a double rigid sole, which in turn will produce the curve of the plantar arch.

2. Orthopedic measures are very essential from the standpoint of postoperative care and every means should be used in order to give a movable tibiotarsal articulation.

3. Operative means. Since the inversion is primarily due to mechanical factors, attempts are made to do away with these factors. The answer to the problem seems to be the re-establishment of the combined action of the antagonistic muscles at the tibiotarsal articulation. A lengthening of the tendo Achillis is carried out in some cases. The anterior tenosuspension of the calcaneus is primarily done by passing the tendons through a tunnel in the anterior part of the calcaneus. Physiological principles must be maintained in order to get a good functional result. The good points of the anterior tenosuspension are: (1) it is opposed in part to inversion of the stump; and (2) it permits a suitable working stump with an almost normal gait.

In the technique of the anterior tenosuspension of the calcaneus each of the individual tissues involved must be dissected and isolated to make a more spacious plantar fragment possible. Care must be taken in making the dorsal incision not to cut the extensor tendons. Each of the tendons is marked with a thread of catgut. The typical Chopart disarticulation is then carried out with the tendons raised and out of the field of operation. A hole is

drilled through the anterior portion of the calcaneus from 3 to 4 mm. behind the anterior articular surface and a gutter is made on the head of the astragalus, vertical in direction, for the tendons of the extensor proprius of the great toe and of the anterior leg. These tendons are passed through the tunnel to the side opposite their origin and then sutured well up on that side to the opposite tendon. During operation the foot is to be maintained in flexion of about 80 degrees. The flaps are sutured.

The authors believe the use of the technique just described, with postoperative care and prostheses, will make poor results a thing of the past.

RICHARD J. BENNETT, JR., M.D.

## FRACTURES AND DISLOCATIONS

**Van der Ghinst, M.: Fractures of the Plateau of the Tibia** (Les fractures du plateau tibial). *J. de chir.*, 1940, 55: 97.

Van der Ghinst defines the plateau of the tibia as that part of the bone which lies above a horizontal plane passing through the lower border of the anterior tuberosity of the tibia, with the exception of the spines of the tibia. The author considers the term "tuberosity" or "plateau" to be preferable to the term "condyle" to designate this portion of the tibia.

There are many different types of fracture of the plateau or tuberosity of the tibia; they are best classified into two main groups, linear fractures and crushing fractures. Each of these two groups includes several varieties. Lesions of the meniscus occur in 20 per cent of these fractures. Whether caused by a direct or an indirect force, fractures of the plateau of the tibia are always due to a movement of hyperadduction or hyperabduction, the resistance of the lateral ligaments to elongation being greater than that of the bone to pressure. Both tuberosities may be fractured, either by a crushing force involving both simultaneously, or by a crushing fracture of one tuberosity and a fracture *en bloc* of the base of the other; the latter is due to extreme hyperadduction.

The most important symptoms of fracture of the tibia are the lateral movements of the limb and the formation of hemarthrosis; the degree of disability depends upon the site and extent of the fracture. Deviation of the limb in valgus or in varus is usually noted. Roentgenological examination is necessary for exact diagnosis; roentgenograms should be made from the front, in profile, and obliquely.

In treatment, closed reduction is often effective, with immobilization of the limb on an inclined plane and in a position of overcorrection; in some cases continuous extension is employed. Open reduction is not indicated unless closed reduction fails. In linear fractures, replacement of the fragment in correct position and fixation with a metal prosthesis is indicated; in crushing fractures bone grafts are necessary to replace the loss of bone substance. Immobilization must be maintained for from eight to twelve weeks according to the case; recovery is slow and depends to a great extent upon the co-operation of the patient for satisfactory functional results.

At the St. Antoine Hospital of Brussels, 21 of 36 cases of fracture of the plateau of the tibia have been followed up, but 1 of these for only a few months after the accident; in 16 of the remaining 20 cases, the results are satisfactory, and in 4 they are poor.

ALICE M. MEYERS.

# SURGERY OF THE BLOOD AND LYMPH SYSTEMS

## BLOOD VESSELS

**Funck-Brentano, P.: The Differential Diagnosis of Arterial Emboli of the Legs** (Le diagnostic différentiel des embolies artérielles des membres). *Presse méd.*, Par., 1939, 47: 1569.

In a discussion of the differential diagnosis of arterial emboli the author asserts that the diagnosis of an arterial embolus is often very difficult to make. In cases of acute arterial occlusion the diagnosis of the pathological cause of the ischemia depends upon the acuity and beliefs of the clinician. According to the teachings of Mars, the embolus in its different modalities may often be the cause of the pathological changes. However, it is relatively rare that this etiological embolus can be confirmed. According to Fontaine the large dimensions of certain clots and the frequency of recurrence after embolectomy indicate that quite often a thrombus has been mistaken for an embolus. The author agrees with Langeron that the embolus is the rarest cause of arterial obliteration. FREDERIC W. ILFELD, M.D.

## BLOOD; TRANSFUSION

**Rostock, P.: Hemostasis and the Replacement of Blood** (Blutstillung und Blutersatz). *Med. Welt*, 1939, p. 1331.

In order to apply proper and useful measures for hemostasis in injuries one must have clear conceptions about spontaneous hemostasis. There are three processes that enable the body to cause a hemorrhage to stop: (1) the contraction of the musculature of the vascular wall; (2) the rolling-in of the injured intima, and (3) the secondary thrombosis at the site of the injury. As a result of the irritation of the injury of the blood vessel the musculature contracts up to the next higher site of the division of the blood vessel, as a result of which the vascular lumen is constricted up to occlusion. This process is of predominant importance in spontaneous hemostasis. The second factor is the rolling-in of the intima at the vascular wound, as a result of which the transverse diameter of the bleeding vessel is diminished in a purely mechanical way. This effect is the least with a smooth cut, but very decided in crushing and tearing of the blood vessel, and for this reason there is no escape of blood in an avulsion of an extremity. The rolling-in of the intima results in such a way that the wound surface comes to lie toward the lumen of the vessel, and the stimulus for the thrombosis arises from this open wound site. Together with its excretion of fibrin and later organization by connective tissue, this is the important prerequisite for the later definitive cicatrization of the vascular injury, but plays only a very subordinate part in the process of primary hemostasis.

For the practical measures in the treatment of an acute hemorrhage, the provisional and the final hemostasis must be kept apart. It is not necessary nor indicated, as still often is done, to tie off the affected extremity in every hemorrhage. Parenchymatous hemorrhages usually cease spontaneously after a short time, and covering with sterile gauze suffices. Venous hemorrhages, no matter how severe they are, always cease with a compression bandage when the body is laid flat and the extremities are elevated. In arterial hemorrhages the cessation of the escape of blood can be achieved by compression of the artery with finger pressure at the known sites. With the smaller vessels from five to ten minutes of pressure usually suffice to occlude the source of the hemorrhage. If the bleeding does not stop after this time, only then the application of an Esmarch bandage is indicated. However, it must be drawn tightly so that the arterial flow is truly stopped, as otherwise the bandage acts statically and increases the hemorrhage. The bandage must never be applied longer than two hours, not even if a definitive hemostasis has been impossible within this time. It may be hoped that within this time the opened blood vessel has become occluded by the automatic aid of the body, even though the conduction of stimulation in the vascular tube has been disturbed by the application of the Esmarch bandage. The definitive hemostasis results from ligation of the vessel at the site of its injury. In the case of the popliteal artery, a vascular suture, possibly together with a free transplantation from the saphenous vein, should be done instead of a ligation, so as to avoid a threatening gangrene. Stimulants are indicated and allowed only after the final hemostasis has occurred.

In connection with marked losses of blood, measures for their replacement should be taken. In the absence of alarming conditions the administration of warm fluids by mouth or rectal drop infusions suffice. Autotransfusion has a limited purpose; it is applicable only for two hours, and after that the blood flows back into the legs that have been made bloodless in a more marked degree and thus a new deficiency of blood occurs in the rest of the body. A transfusion with normosal solution or with totofusin is also occasionally recommended, possibly with the addition of stimulants. However, if the loss of blood is so great that the erythrocytes still present are not sufficient for the necessary gaseous metabolism, the transfusion of sufficient amounts of living blood from another person may receive consideration. The transmitted erythrocytes remain functionally active up to thirty days—a period of time sufficient for the body to supply its own replacement. With a proper selection of a donor dangers are no longer to be feared. The former method for the avoidance of coagulation with the use of sodium citrate is now replaced by the use of vetren, which is derived from

the liver. The blood transfusion not only replaces the loss of blood and prevents death from exsanguination, but also acts as a hemostat and forms a marked stimulant for the hematopoietic organs of the body, the activity of which stimulates them greatly to the autogenous replacement of the lost blood.

(Bode). Louis Neuwelt, M.D.

**Edwards, F. R., Kay, J., and Davie, T. B.: The Preparation and Use of Dried Plasma for Transfusion.** *Brit. M. J.*, 1940, 1: 377.

The authors note that the formation of blood banks has made available a considerable supply of plasma for therapeutic use. It is the plasma element that produces the desired effect in many blood transfusions which are given. It is the plasma proteins combined with fluid which appear to be responsible for the resuscitative action in wound shock, postoperative shock, and burns. Further advantages of the plasma are that it will keep indefinitely, and for its administration no grouping of the recipient is necessary.

A brief consideration of the physiopathology of plasma proteins is given. The method of preparing plasma is discussed. The plasma should be kept in a refrigerator at 4 degrees C. Under these conditions of storage, the plasma will keep indefinitely.

Although the administration of pure plasma has been satisfactory, it was felt that if the product could be dried the problem of storage and transportability could be greatly simplified. Plasma may, without detriment, be heated to 33 degrees C. At this temperature the low vacuum produced by an ordinary standard filter pump will cause it to boil. To prevent the frothing that occurs during ebullition a continuous-feed plasma drier has been used. When completely dried, the granules are crushed to a fine powder and are stored in ampoules.

One hundred cubic centimeters of citrated plasma gives about 8 gm. of the dried product, which is a pale yellow crystalline powder that dissolves readily in warm water. The reconstituted plasma is indistinguishable in appearance from the original product. It can be stored at room temperature and will apparently remain effective indefinitely.

The rationale for the administration of plasma in wound shock, postoperative shock, incipient pulmonary edema, burns, nephritic edema, and malnutritional edema is discussed. Twenty grams of dried plasma dissolved in 250 c.cm. of distilled water, or 500 c.cm. of 5 per cent glucose in distilled water are equivalent in plasma-protein value to 1 pt. of citrated blood.

The experience of the authors in transfusion is not great enough to fully assess the value of dried plasma, but the anti-shock property of this substance appears to be comparable to that of whole blood. It seems to be ideal for use in cases of emergency in which no supply of blood is easily available, and in war surgery. Herbert F. Thurston, M.D.

# POSTOPERATIVE ATELECTASIS AND RELATED PULMONARY COMPLICATIONS

## Collective Review

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A CONSIDERABLE number of articles on postoperative pulmonary complications have been published since the careful review of Mathes and Holman (69). These papers have dealt largely with clinical observations and the therapy of these conditions. Several important papers of an experimental nature, however, have appeared, which in general tend to support the obstruction theory of the development of atelectasis and postoperative pneumonia. The importance of the problem is obvious, and only by constant vigilance and attention to detail can these conditions be prevented. Gray (45) has stated, "Pulmonary complications constitute the greatest single hazard in abdominal surgery, and if death cannot be ascribed to them, not infrequently they reduce the actual defensive forces so that a fatal outcome ensues when recovery might otherwise have followed."

The predominant postoperative pulmonary complication is atelectasis, and the related conditions include bronchitis, massive collapse, and postoperative pneumonia. It is apparent that to include a discussion of certain other affections of the lung occurring postoperatively would necessitate much greater length than can be given here, and indeed would detract from the main point of this review, namely, the study of those conditions occurring within the first four or five days after operation. Veal (100) has indicated that pulmonary embolism and infarction in one sense are not pulmonary complications at all, but vascular accidents resulting from surgery which are not due, strictly speaking, to a pulmonary condition. For this reason, pulmonary embolism and infarction, fat embolism, pulmonary abscess, gangrene, and bronchiectasis are not included in this review.

The history of the development of the present concept of postoperative pulmonary complications forms an interesting chapter in the history of medicine. This aspect has been reviewed many times (Bowen, 14) and only a few of the high points should be recalled.

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With the advent of surgery and especially with the discovery of anesthesia, pulmonary complications were recognized as common sequelæ to operation. These were referred to as "ether pneumonia," but with the development of other types of anesthesia it was observed that similar complications occurred with equal frequency when they were used. Thus, it was soon demonstrated that the anesthetic *per se* was not the primary cause of the trouble. Jorg (60) in 1823 described the presence of incompletely aerated lungs in the newborn and coined the word "atelectasis" from the two Greek words, "ateles" meaning imperfect and "ektasis" meaning expansion. Traube (95) showed in 1844 that atelectasis following section of the vagus or recurrent laryngeal nerves was due to the entrance of buccal secretions into the air passages. Gairdner (43) recognized that collapse of the lung occurred in a variety of cases, and believed bronchial obstruction to be the primary cause. Lichtheim (66) in 1879 proved beyond any doubt that collapse of the alveoli was due to absorption of the alveolar air into the blood stream. It was not until the term was revised by Pasteur (75, 76), Bradford (15), and Scrimger (85) that such a condition was considered in the literature regarding postoperative pulmonary complications. Bibergeil (13) following a comprehensive study of these conditions stated, "It is due in part to the instinctive dread of pain and in part to protective reflex inhibition. The tendency to inflammation is further aggravated by the difficulty of effectually clearing the lungs of offending matter by coughing."

Elliott and Dingley (39) in 1914 studied a series of 11 cases of massive collapse following operation and concluded that this condition was secondary to bronchial obstruction. They recommended deep breathing and coughing as the preferred treatment, and suggested pneumothorax as a therapeutic consideration. Cutler and his associates (34, 35) subsequently published a series of papers on this subject, the thesis of which was that emboli arising from the operative site and passing to the lungs are the chief etiological factor. About this time Whipple (104) analyzed a series

of 97 cases of "pneumonitis" occurring among 3,719 patients operated upon in the Presbyterian Hospital, New York City, during the years 1915 and 1916. He listed the following predisposing factors:

1. Local inflammations in the upper respiratory tract and factors favoring them.
2. Vasomotor changes causing a congestion of the pulmonary vessels.
3. Factors inhibiting the normal thoracic and abdominal respiratory movements and favoring atelectasis and hypostasis in the lungs.
4. Local or general infections elsewhere than in the respiratory tract.
5. Debilitated states resulting in a lowered natural or acquired immunity to the particular organism inciting the pneumonia.
6. Factors increasing the virulence of the inciting organism.

The first four of these factors cover most of the predisposing causes of pulmonary atelectasis as we view it today. Subsequent work has elaborated chiefly on the factors in Group 3 (Snyder, 89).

It was Whipple's belief that these conditions were the result of extension of infection from the upper respiratory passages into the lung with the production of inflammation or pneumonitis.

Jackson and Lee (57) produced atelectasis in dogs by the intrabronchial injection of mucus obtained from a patient with pulmonary disease, and then obtained rapid re-inflation of the collapsed portion of the lung by removing the plug bronchoscopically. Coryllos and Birnbaum (28, 29, 31, 32) in an extensive experimental study demonstrated that bronchial occlusion was the primary cause of atelectasis. They showed that subsequent absorption of air distal to the plug occurred on a purely physical basis, and if virulent organisms were present in the retained secretions a cellulitis and rapidly spreading infection resulted unless prompt removal of the occluding mucus plug occurred. Thus, they contended that postoperative pneumonia was a condition secondary to atelectasis.

### PHYSIOLOGICAL CONSIDERATIONS

The normal lung is expanded by hydraulic traction on the visceral pleura by the outward moving thoracic walls (Andrus, 2). Thus, the lungs play only a passive rôle in respiration and are subject to changes in the chest wall and diaphragm. During inspiration the thoracic cavity is increased in all diameters; that is, the anteroposterior dimension is increased by elevation of the sternum and ribs; the transverse diameter is increased by elevation of the ribs, the so-called "bucket-handle movement"; and the vertical diameter is increased by descent and forward motion of the diaphragm. The portions of the lung which are expanded directly are those in contact with freely movable boundaries of the thorax, namely, the sternum, ribs, and diaphragm. Macklin (68) has shown that the lung root moves downward, forward, and laterally during inspiration, and that the bronchial tree is elongated. With descent of the diaphragm there is a decrease in intrapleural pressure which is considerably greater in the supradiaphragmatic region than in other areas (Best and Taylor, 12). It is estimated that the action of the diaphragm is responsible for about 60 per cent of the ventilation of the lung normally. Hoover (54) has indicated that the diaphragmatic movement accounts almost entirely for the ventilation of the lower lobes. During respiration the diaphragm moves up and down like a piston and changes its shape only slightly. The costosternal part moves downward and forward and pushes the abdominal viscera before it. The abdominal wall distends, but when resistance is offered by the abdominal muscles, the downward movement of the viscera is hindered. At this point the force of the diaphragm is spent in raising the lower ribs to which it is attached (Best and Taylor, 12). Under normal conditions the excursion of the anterior abdominal wall is a direct measure of phrenic excursion. It is obvious, therefore, that conditions which alter intra-abdominal pressure or abdominal-wall tonus, such as distention, peritoneal irritation, abdominal-wound pain, and associated spasm, will influence the diaphragmatic excursion and ventilation of the lung (Patey, 77; Carlson, 23, 24; Beecher, 8; Capelle, 22). When these factors produce a decrease in the abdominal component of respiration, a tendency toward compensation by the thoracic components of respiration is noted (Carlson, 23, 24; Beecher, 8).

Many authors (Head, 48; Churchill and McNeil, 26; Powers, 78; Patey, 77; Carlson, 23, 24; Beecher, 8; and others) have reported a fall in the vital capacity which occurs after abdominal operations. This decrease is greatest in operations on the upper abdomen and the level following operation in this area usually ranges from 20 to 40 per cent of the normal for the particular individual studied during the first few days after operation. Return to normal is gradual so that the pre-operative level is usually reached by the tenth or twelfth day. Khromov (61) found that the fall in vital capacity was less and the return more rapid if the patient was allowed out of bed early.

Whereas inspiration is an active phenomenon, expiration during quiet breathing is entirely passive. The thoracic framework, through its own weight, together with the elastic recoil of the lung and relaxation of the diaphragm, allows the lung to resume its former position. With fluctuations of the diaphragm, alterations in both intrapleural and intra-abdominal pressures occur which account in a large measure for movement of blood through the large veins back to the right heart (Wilson, 105). There is, therefore, a definite circulatory function ascribable to respiration and especially to diaphragmatic excursion. This has been referred to as the "pumping action" of the diaphragm and its importance as regards postoperative venous stasis, thrombosis, and embolism has been stressed. Frimann-Dahl (42), however, has noted that the decrease in diaphragmatic excursion was greatest on the first postoperative day, while the slowing-up of the venous return occurred later, and in fact the curve of each seemed to be in opposite directions. He concluded that the diaphragm was not the chief factor in the slowing-up of the venous circulation.

It should be noted that an interrelationship between ventilation and circulation of the lung has been quite conclusively demonstrated by numerous workers. Coryllos and Birnbaum (30) stated, "circulation and ventilation of the lung are parallel functions; where ventilation is impaired circulation is decreased and conversely." They found progressive impairment of circulation in the atelectatic lung which was due to collapse of the alveoli and not to capillary thrombosis or capillary compression by the alveolar exudate. Adam and his co-workers (1) found a decreased volume of blood flow associated with passive congestion and an ideal situation for bacterial invasion in massive atelectasis. Thus it is clear that hypoventilation and atelectasis affect profoundly both the systemic and pulmonic circulation. Overholt (74) regarded pneumoperitoneum as a possible cause of a high diaphragm after operation, but subsequent investigators (Beecher, Bradshaw and Lindskog, 10; Carlson, 23, 24) have reported that the degree of pneumoperitoneum which would be required to produce this effect would have to be far in excess of that resulting from laparotomy. Positive pressure, however, such as that produced by distention of the gastro-intestinal tract, causes a definite impairment of respiratory exchange. It is conceivable also that distention might cause a secondary decrease in the diaphragmatic excursion by virtue of the fact that internal pressure on the wound might produce pain sufficient to bring about a reflex splinting of the diaphragm.

The condition frequently called "hypoventilation" has been repeatedly demonstrated after abdominal operations (Patey, 77; Carlson, 23, 24; Beecher, 8). This results from a number of factors which have already been mentioned. Henderson (49) has stressed the rôle of tonus in maintaining the normal capacity of the lungs. It is the tonus of the respiratory muscles that normally keeps the thorax and, thus, the lungs expanded, and prevents atelectasis. He believes that loss of tonus not only affects the lungs, but also profoundly affects the whole organism because of the dependency of the so-called "venopressor" mechanism on tonus in all muscles. This mechanism is the chief factor in the return of blood to the right heart.

With a decrease in tonus which may follow a surgical operation, physical injury, anesthesia, or severe illness, a diminution in the size of the thoracic cavity and a partial deflation of the lungs are produced. This condition has been called "collapse without symptoms" by Beecher (9), who found it after more than 80 per cent of laparotomies.

Thus the groundwork for certain essential factors leading up to actual obstruction of the bronchial tree is set. At this point, secretions which have been retained in the bronchioles or bronchi produce obstruction to the passage of air distally. If obstruction persists, rapid absorption of air into the blood stream occurs. The air from the occluded area is absorbed exactly as from any other body cavity. As the air is absorbed the lung is gradually collapsed under the pressure of the atmosphere bearing down through the trachea and bronchi into the other lung and by elevation of the diaphragm by the pressure of the atmosphere upon the abdomen. This appears to be the complete explanation of why it is that a plug in a main bronchus results in collapse of the lung on that side and an expansion of the other lung to fill part of the other space (Henderson, 49). That there is essentially no difference between lobar and lobular collapse is stressed by Coryllos (27). Wangensteen (101) believes, however, that although the lobular type of atelectasis results chiefly from the presence of thick viscid mucus in the tracheobronchial tree, the temporary ablation of the diaphragmatic component of respiration following abdominal operation is the most important factor in the genesis of lobar or massive atelectasis.

The possibility of reinflation of collapsed lobules by the passage of air through the interalveolar pores (Kohn) from adjacent air-containing alveoli has been shown by Van Allen and his collabora-

tors (98, 99). Thus, unless the "collateral respiration" of the obstructed portion of the lung is blocked by inflammatory exudate and edema, areas of lobular atelectasis may be reinflated by this mechanism. It is clear that complete lobar obstruction does not allow this mechanism to operate. Whether the interalveolar pores are normal structures or artefacts due to stretching or tearing of the alveolar membrane from various causes has not been settled to the satisfaction of all investigators. The latter view, however, is held by most anatomists (Larsell, 64). It would seem that this mechanism adequately explains the striking results obtained clinically by hyperventilation and coughing.

Band and Hall (6) showed experimentally that three factors were necessary for the development of atelectasis. These were (1) an intrabronchial content of a definite viscosity; (2) abolition of the cough reflex; and (3) limitation of respiratory movement. This work confirmed much of that done by Coryllos and Birnbaum, and their concept of bronchial obstruction with secondary pulmonary collapse is almost universally accepted as the predominant postoperative pulmonary complication (editorial *J. Am. M. Ass.*, 36).

Bacterial invasion of the collapsed area proceeds usually from organisms contained in the mucus plug. This results in an inflammatory process, to which Whipple (104) applied the descriptive term "pneumonitis." A great variety of organisms may be cultured from the involved area. Nearly always these are derived from the upper respiratory passages and in the greater percentage of the cases pre-operative cultures of the nasopharynx will yield the same organism that predominates in the affected lung (Sutliff and Steele, 91). The severity of the symptoms will depend upon the following factors: (1) the amount of the lung collapsed and the displacement of the mediastinum and traction on the great vessels which results; (2) the degree of pneumonia in the atelectatic lung; and (3) the type and virulence of the organism causing the pneumonia (Schindler and Gnagi, 82).

The lungs have been called the best drained organs in the body. The normal mechanisms for keeping the tracheobronchial tree patent are the cough reflex, the ciliary activity of the bronchial epithelium, and the peristaltic action of the bronchial air passages. With inspiration a definite dilatation of the bronchial tree occurs and with expiration the reverse is noted. Hyperventilation increases these actions and consequently may result in the freeing of obstructing plugs from the bronchial wall.

Jackson has called the cough reflex "the watch dog of the lungs," and its importance in clearing the respiratory passages cannot be overemphasized. It is a common observation that following abdominal operations, particularly of the upper abdomen, the patient is unable to cough effectively because of pain in the operative wound. Not only is this a factor in decreasing the effectiveness of cough but the degree of hypoventilation and the lowered vital capacity after operation require that much of the inspired air be utilized in sweeping out the dead air space rather than in evacuating the mucus plug. In this respect ineffective coughing, postoperatively, has the same basis as "collapse without symptoms" which has been described by Beecher (9). The undependability of cough in the removal of the tracheobronchial contents has been stressed by Brown and Archibald (17). They found that many times cough would spread the contained material deeper or into the other portions of the lung. Likewise, material contained in the air passages which stimulates cough normally will not produce cough if retained for some time because a tolerance to the foreign material is gained and a temporary loss of the cough reflex results. Jackson (55) showed that material in the finer divisions of the tracheobronchial tree and the alveoli excites less cough than is noted under similar conditions in proximal portions.

Posture, likewise, plays an important part in effective coughing. The semi-Fowler position which is so popular during the postoperative course aids somewhat in the ventilation of the chest, but a disadvantage is the tendency for secretions to gravitate to the most dependent portions of the lung. Here they produce obstructive and inflammatory phenomena, usually in the lower lobes. Faulkner (40) has termed this "internal drainage." On the other hand, if the Trendelenburg position is utilized, or the lateral position with elevation of the foot of the bed, postural drainage of the secretions is effected and they are brought from the relatively less sensitive areas to the larger ramifications where cough will result in their evacuation. Similarly, the lateral position with the involved lung uppermost will provide postural drainage of its bronchial tree. The danger when the latter position is maintained is the introduction of secretions into the uninvolved dependent lobes. This can be obviated by frequent changes in position. Haight (47) has indicated the following reasons for the retention of secretions: (1) the inability or unwillingness of the patient to cough effectively; (2) the lack of application of helpful measures for aiding cough and

expectoration; and (3) improper instruction of the patient regarding the necessity for effective cough and expectoration.

Henderson (49), as previously noted, has stressed the importance of the venopressor mechanism and its failure during the state of postoperative depression. He believes that this is one of the chief predisposing factors in the development of postoperative pulmonary complications. Moon (70), who has made extensive studies of the pathology of shock, suggests that postoperative pneumonia is a manifestation of a sublethal degree of shock. He observed secondary pneumonia in hyperemic edematous lungs of patients who died several days after extensive surgical procedures. Blood studies on these patients showed marked degrees of hemoconcentration, which indicated that the mechanism of shock was operative. The post-mortem findings were comparable to the pulmonary changes noted in many other conditions and the essential pathological pattern of shock was present in all. This consisted of congestion, stasis, and edema of the lungs. Takacs (92) stressed the rôle of the carbon dioxide-oxygen balance in maintaining the central control of respiration. He found that sudden collapse of the lung results in a profound upset in the carbon dioxide-oxygen exchange and an inability of the respiratory center to respond promptly. This would seem to be of particular importance in lobar or massive collapse. In addition to the usual factors which he accepts, Sauerbruch (81) suggests that a reflex nervous influence may excite pathological changes in the lung after upper abdominal operation. This condition might be analogous to the postoperative atony of the gastro-intestinal tract and is due to irritation of the abdominal vagosympathetic system. Zukschwerdt and Lezius (106) have suggested that changes in tonus of the sympathetic nervous system may produce constriction of the bronchi. The possibility that these changes are due to toxic products liberated from the field of operation is inferred in their writings. Although the literature of previous years has contained frequent references to the rôle of allergy in pulmonary complications, most recent authors have given little space to its consideration. Lueth (67) claims it is a frequent etiological factor.

## PATHOLOGY

The atelectatic portion of the lung is shrunken, airless, firm, gray in color, and sinks in water (Snyder, 89). The bronchi are often filled with tenacious densely adherent mucus. Microscopically the alveolar walls are engorged with blood, and the alveolar spaces are flattened and small. They may contain a homogeneous mucoid substance and a variable amount of cellular exudate. Adam and his coworkers (1) observed that shrinkage of tissue with atelectasis produces a decreased cross section of the vascular bed as well as marked tortuosity of the vessels.

The lung in postoperative pneumonia is very dark violet in color and a thick mucopurulent secretion can be made to exude from the bronchioles on compression. The alveolar surfaces are closely approximated and the alveolar spaces are obliterated. The alveolar capillaries are collapsed and the arterioles are dilated. A fibrinopurulent exudate is present in the bronchioles (Starr, 90).

Moon, who has suggested the rôle of shock in postoperative pneumonia, notes that the lungs are heavy, wet, and of increased density. The areas of consolidation may vary greatly in size, distribution, and number. The sections show marked engorgement of the capillaries and venules, and albuminous fluid filling the alveoli. It is possible that the type of changes described by Moon (70) are the result of vascular changes primarily, while the picture produced by atelectasis and secondary pneumonia is due to changes intrinsic to the lung. Coryllos believed that atelectasis was the common factor in the development of postoperative pneumonia as well as primary pneumonia.

Zukschwerdt and Lezius (106) emphasize the importance of the mediastinal shift and traction on the great vessels in massive collapse. They point out that it is impossible to demonstrate these changes at autopsy unless the trachea is ligated before the chest is opened.

## BACTERIOLOGICAL CONSIDERATIONS

The presence of infection in the upper respiratory passages has long been recognized as a predisposing factor in the development of postoperative pulmonary complications. It is now universally accepted that all elective surgery should be deferred for at least a week, or preferably two, after a cold has cleared up. Also, operation in the presence of a rhinitis, sinusitis, pharyngitis, laryngitis, dental infection, or any similar infectious condition should be regarded as extremely hazardous. All efforts should be made to clear up both acute and chronic infections in the upper, as well as the lower, respiratory passages before surgical procedures are carried out.

Most healthy individuals harbor pneumococci and streptococci in their oronasal secretions (Band and Hall, 6). Coryllos found Group IV pneumococci in about 40 per cent of his patients and believed that the great viscosity of the bronchial

secretions, so characteristic of bronchial stasis, results from the rapid growth of the pneumococci. Thus, the viscosity of the bronchial secretions is sufficient to produce obstruction of the small and even the large bronchi. The more virulent the pneumococci are, the greater is the viscosity of the exudate formed (Levin, 65).

Several investigators (quoted by Sutliff and Steele, 91) have determined that pneumococci can be found in the throats of one-half of the normal people given a single examination, and as the number of examinations and the period of time over which they extend are increased the proportion found to harbor pneumococci is also increased to nearly 100 per cent. More than one strain may be present, and changes in the strain present may occur frequently. Other organisms, such as the beta hemolytic streptococcus and Friedlaender's bacillus, are less often present.

Turnbull (97) believes staphylococci and streptococci are usually associated with the lobular type of atelectasis, and if anaerobic organisms are imprisoned, destruction of tissue may follow the pneumonitis with the production of an abscess.

Sutliff and Steele (91) studied the interrelationship of infection and hypoventilation. They took repeated cultures of the pharyngeal flora on 16 patients before and after abdominal operation. Fifteen had upper abdominal operations. They distinguished three types of cases according to the respiratory pathogens found.

1. Three cases showed no pneumococci at any time. The patients all manifested the minimum of postoperative pulmonary changes, called hypoventilation.

2. Six cases showed pneumococci or beta hemolytic streptococci constantly or intermittently but with no relationship to a pulmonary complication. A diagnosis of a pulmonary complication was made in each.

3. A group of 7 cases revealed the pneumococcus, or, in one instance, a mouse virulent alpha hemolytic streptococcus after operation coincidentally with pulmonary changes.

These authors believed that the postoperative changes in the physiology of respiration and circulation were related to the development of bronchitis, bronchopneumonia, and collapse to such an extent that they favored the bacterial invasion of the lower respiratory tract. Patients who had no respiratory pathogens in the pharynx had the least pulmonary changes, and those who harbored such organisms showed thoracic changes of varying degrees. Sutliff and Steele concluded that the pulmonary signs were the result of the presence of the organisms, and the severity of the symptoms was proportional to the virulence of the organisms.

These studies indicate that the primary change following operation is hypoventilation and this permits bacterial invasion and growth.

In 13 of a series of 21 cases of postoperative pneumonia reported by Hinshaw and Moersch (52), the pneumococcus appeared to be the causative organism. There were 2 cases of Type 6, and 1 each of Types 1, 3, 10, 13, 15, 16, 17, 20, 23, 24, and Group E. These authors stressed the point that although the types of pneumococci in postoperative pneumonia vary greatly, sulfapyridine seems to be effective in all.

### THE INCIDENCE OF POSTOPERATIVE PULMONARY COMPLICATIONS

There has been considerable discrepancy in the literature regarding the frequency of postoperative pulmonary complications. Cutler (34, 35) stated that they occurred after about 2 per cent of all operations, 4 per cent of all laparotomies, and 8 per cent of all upper abdominal operations. The mortality is said to be 0.6 per cent or 1 case in every 200 (Editorial, *J. Am. M. Ass.*, 36). Brunn and Brill (19) found atelectasis in 4.8 per cent of their series. Snyder (89) reported an incidence of 1.9 per cent. Eliason and McLaughlin (37, 38) reported that from 1.5 to 3.5 per cent of all surgical cases developed pulmonary complications. King (62) reported 3.7 per cent, 5.2 per cent, and 6.8 per cent in various years, and emphasized the fact that the greater the interest in the condition and the more it was studied, the greater would be the number of cases diagnosed. Rovenstine and Taylor (80) reported 6 per cent minor and major pulmonary complications in a large series of cases. Sutliff and Steele (91) were able to demonstrate changes roentgenographically, by physical examination, or by both methods in 69 per cent of a small series of cases. Nearly all of the patients had had upper abdominal operations. Beecher (9) showed "collapse without symptoms" in over 80 per cent of the patients subjected to abdominal operation which he studied. Sutliff and Steele suggest that most observers have reported only cases of maximum severity and have determined the incidence on this basis.

Brock (16) objects to the use of the term "massive collapse" because it has resulted in a lack of recognition of atelectasis of a patchy or lobular type unless the signs and symptoms are marked. Many times the signs may be minimal and cardiac, or mediastinal displacement cannot be demonstrated. It is in these cases particularly that roentgenographic examination is valuable.

For these reasons it would seem illogical to classify all cases into a single group, but rather they should be separated into all gradations, including hypoventilation, bronchitis, atelectasis (lobar and lobular), and pneumonia.

In any event, diagnosis of these conditions depends largely on the "atelectasis consciousness" of the individuals who care for these patients. Sewall (86) has urged the profession to "think atelectasis," and as this idea becomes more prevalent the diagnosis will be made earlier in the course of the disease and therapeutic measures to correct it can be invoked. Thus the more serious complications may many times be prevented.

Burford (20) has stated that the problem of pulmonary complication following operation not on the abdomen in his experience has always been negligible. Males are said to be affected twice as frequently as females. This is due, presumably, to the fact that males are predominantly abdominal breathers and consequently abdominal operation results in greater damage to the respiratory apparatus in men than in women. Operations on the stomach and the biliary tract as well as on the spleen are followed by pulmonary complications in a very high percentage of cases. Splenectomy is said to produce lung complications in 25 per cent of the cases (Apgar, 4). Rovenstine and Taylor (80) observed that the seasonal-incidence variation depends on the presence of respiratory infections and that the anesthetic agent *per se* exerted no marked influence. The anesthetic technique did seem to play a rôle. The duration of the operation and the operative procedure were likewise definite factors influencing the pulmonary morbidity. In operations lasting one-half hour or less the incidence was 2.9 per cent and increased progressively for each half hour to 30 per cent for operations lasting from three to three and one-half hours (Taylor, Bennett, and Waters, 93).

Schmidt and Waters (83) report the following figures on a very large series of cases:

MAJOR RESPIRATORY COMPLICATIONS

| Anesthetic Agent | Cases | Per cent |
|---|---|---|
| Cyclopropane | 10,044 | 1.10 |
| Ether | 4,462 | 2.37 |
| Nitrous oxide | 2,338 | 1.02 |
| Ethylene | 1,044 | 1.05 |
| Spinal | 1,340 | 1.34 |
| **Type of Operation** | **Cases** | **Per cent** |
| Orthopedic (except spine and amputations) | 3,241 | 0.24 |
| Upper abdominal laparotomies | 1,131 | 7.43 |
| Lower abdominal laparotomies | 2,762 | 2.67 |
| Gynecological and Obstetrical (except laparotomies) | 3,148 | 0.16 |

CLINICAL PICTURE

1. Bronchitis. This is a common complication after operation, but frequently progresses to more serious complications. Consequently the recorded incidence is low since many of these cases are reported as atelectasis or pneumonia. King (62) states that the incidence is 3 per cent. The patient develops a simple productive cough with fever but with no abnormal physical signs beyond a few râles. Resolution occurs rapidly with no evidence of permanent damage. Starr (90) believes it is due to a circulatory imbalance of the lung and if encountered in the normal patient it infers incorrectly administered anesthesia. In patients suffering from precedent respiratory infection, debility, or sepsis, it may occur following even well administered anesthesia. The danger lies in allowing bronchitis to proceed to a more serious respiratory complication.

2. "Collapse without symptoms." This condition has been described by Beecher (9) and discussed by Henderson (49). Sutliff and Steele (91) have referred to it as "hypoventilation." Beecher found it in 82.9 per cent of a series of laparotomies. He believes that this is a diffuse and partial collapse rather than a local and complete collapse. There was no evidence of collapse on physical or x-ray examination, yet measurements of the subtotal air showed a significant and consistent decrease after laparotomy. He states that some of the usual postoperative manifestations may be due at least in part to its development. These manifestations are principally a rise in pulse and temperature and the typical shallow, rapid respirations.

3. Atelectasis. The signs and symptoms of atelectasis usually appear within the first forty-eight hours after operation but may be deferred until the fourth or fifth day. Moore (71) stated that any patient developing a sudden or unexpected elevation of temperature or respiratory rate after operation should be suspected of having atelectasis until proved otherwise. There is also a tachycardia early which Starr (90) considers an important diagnostic factor. The earlier the onset of symptoms the more serious the subsequent features and the more rapid the march of symptoms are likely to be (Starr, 90). Also, the longer a rise in temperature and pulse is delayed after operation the less likely is the cause to be simple atelectasis (Brock, 16). Dyspnea and cyanosis may or may not be prominent. Cough with expectoration of thick tenacious sputum, which is never blood tinged, may be present according to the patient's ability to cough effectively. Brock has emphasized the diagnostic importance of the

cough which he has described as "fruity." It is due to the "gargling" of thick mucopurulent material in the trachea and large bronchi, and the typical, frequent, restrained, ineffective coughing of the patient.

The physical signs in the early stages are notoriously inconstant and variable. Transient physical signs are found in the chest after nearly all upper abdominal operations and a diagnosis of atelectasis is usually not warranted on the basis of the physical signs alone. In the typical case in which collapse involves an area sufficient to produce a mediastinal shift the findings are definite. The expansion of the affected side is limited or absent while that of the opposite side is increased. The apex beat is displaced toward the collapsed side. Bye (21) regards this as the most important physical sign. It will not occur if bilateral collapse is present, or if the mediastinum is fixed. Zukschwerdt and Lezius (106) also emphasize the shift of the mediastinum as a diagnostic point and an indication for urgent therapy by means of artificial pneumothorax. Early there is often hyper-resonance over the affected lung, but later dullness is found. The breath tones are diminished or absent and no râles may be heard in the beginning, but later the breath sounds become tubular or amphoric and moist crackling or bubbling râles may be heard.

Christopher and Shaffer (25) as well as many other authors have stressed the importance of the x-ray examination because of the difficulty of differentiating between collapse and pneumonia by physical signs alone. Roentgenographically there is elevation of the diaphragm and narrowing of the chest on the affected side. An increased obliquity of the ribs and decrease in the size of the intercostal spaces can usually be demonstrated. The trachea, heart, and mediastinum are displaced toward the affected side, and the involved lung tissue shows an increase in density. Warner and Graham (102) as well as Anspach (3) have emphasized the diagnostic value of a triangular shadow with associated displacement of the surrounding structures toward it at the base of the lung as a sign of collapse. The development of bronchiectasis in the collapsed area has been demonstrated when subsequent expansion has not taken place.

4. Postoperative pneumonia. The involvement may be lobular or lobar, but the clinical features are usually those of a severe lobar pneumonia. The temperature remains high, the pulse rises, and the respiratory rate may be markedly elevated. The skin is hot and as a rule sweating is profuse. Cyanosis and cough with expectoration of large quantities of mucopurulent sputum are quite constant features. Pneumococci can usually be isolated from the sputum. Delirium frequently occurs. The signs in the chest are those of consolidation and vary with the stages of the disease. Bergh (11) states that râles appear early in pneumonia and late in atelectasis. The x-ray changes are usually diagnostic.

Lobar pneumonia has been frequently diagnosed postoperatively when only massive atelectasis was present (Brock, 16). Hypostatic pneumonia is usually a terminal event, but retention of secretions, stagnation, and atelectasis may play an important part in its development.

### PRE-OPERATIVE, OPERATIVE, AND POSTOPERATIVE CONSIDERATIONS

Certain precautions taken to prevent the occurrence of postoperative pulmonary complications are particularly effective, as can be logically assumed from considering the foregoing paragraphs on predisposing conditions. Holman (53) has emphasized the fact that a few days spent in preparation for operation usually means days saved postoperatively. The nutritional factors, which previously have been given insufficient attention, are the proper administration of fluids, carbohydrates, proteins, vitamins, and blood. The patient frequently has been on an inadequate diet for an extended period because of his disease and his reserves of these substances have been greatly depleted. Poor wound healing due to a decrease of serum proteins (Ravdin, *et al*, 94) or Vitamin C (Lanman and Ingalls, 63) may lead to wound disruption when associated with a pulmonary complication, and not infrequently may result in a fatal outcome in an otherwise favorable case. Holman points out that the reserves of Vitamins A, C, and D are particularly important in the patient who is subjected to a surgical procedure.

The presence of an upper respiratory infection is an undoubted contraindication to elective operation. Holman indicates that a patient admitted to a hospital and operated upon the following day may be developing such an infection, but the signs and symptoms do not become evident until after the operation. Then a fulminating pulmonary complication appears when the factors of hypoventilation, decreased ability to cough, and irritation of the respiratory passages by the anesthetic are added. This is a strong argument in favor of a period of hospitalization of two or three days before surgery is carried out, particularly in cases which are likely to develop pulmonary complications postoperatively.

Chronic oral sepsis or oronasal infection are likewise important contributing factors to postoperative pulmonary complications and an attempt should be made to place the patient in the best possible condition as regards these infections before surgery is carried out. When chronic pulmonary disease exists every means should be taken to rid the tracheobronchial tree of exudate before operation by means of postural drainage or bronchoscopy if necessary (Holman, 53).

A careful study of the cardiovascular status of the patient should be carried out and if signs or symptoms of cardiac failure are uncovered, digitalization should be completed before operation. The stomach should be emptied by tube before gastric operations to obviate regurgitation and aspiration of its contents while the patient is under anesthesia (Balfour and Gray, 5).

Taylor, Bennett, and Waters (93) have emphasized the close correlation between the preoperative grading of the patient according to the operative risk and the development of pulmonary complications. Brown (18) has discussed three simple methods of evaluating the operative risk. These consist of (1) the breath-holding test; (2) the determination of the pressure ratio (Moot's rule); and (3) the determination of the energy index. These studies provide a valuable guide in foretelling the probabilities of complications and prepare the staff to undertake prophylactic measures immediately after operation, and to be on the lookout for their development.

The rôle of excessive sedation before operation as a cause of pulmonary complications has been repeatedly stressed by various authors (Holman [53] Waters, 103). These drugs are respiratory depressants and consequently should be used with extreme care. Burford (20) suggests that relatively heavier premedication is indicated in the male who is twice as susceptible to pulmonary complications as the female. He advises that the patient be almost asleep when brought to the operating room, and as nearly insusceptible to the stimuli of his surroundings as possible; his metabolic rate should be greatly depressed. The medication should be given far enough in advance to have reached its maximum effect before the anesthetic is started and to be wearing off as the anesthetic progresses. This method of premedication is designed particularly for use with cyclopropane.

It has been held by some that the anesthetic agents play a relatively insignificant rôle in the development of pulmonary complications. Burford points out, however, that the anesthetic affects the results directly through the degree of damage or excessive irritation produced in the respiratory tract and through the degree of depression produced by the anesthetic itself because of excessive relaxation and prolonged action. Frazier (41) reported pulmonary complications in 5.66 per cent of 300 patients given spinal anesthesia, and 9 per cent of a similar series given general anesthesia. Circulatory collapse was more frequent following spinal anesthesia. Schmidt and Waters (83) (see previous table) reported a lower incidence of pulmonary complications following gas anesthesia, chiefly cyclopropane, than after other types. Brock has related Ogilvie's experience with local anesthesia in gastric surgery but in this country this type of anesthesia has not been used widely in abdominal operations.

The danger of massive collapse during or following anesthesia with the rapidly absorbed gases has been pointed out by Jones and Burford (59). They cited 4 cases, 3 of which were fatal and came to autopsy. In each instance massive atelectasis not associated with bronchial obstruction was the only demonstrable pathological finding. These authors, therefore, suggest diluting the anesthetic mixture with either of the relatively inert and slowly absorbed gases helium or hydrogen.

Since the loss of tonus is believed to be one of the prime factors in the development of pulmonary complications (Henderson, 49), cyclopropane appears to have advantages over other anesthetics. It produces a degree of muscular relaxation which can only rarely be exceeded (Burford, 20). The degree of relaxation may be insufficient to satisfy all surgeons, but when it is realized that relaxation is secured at the risk of serious complications, certainly concessions will have to be made, especially in the cases of those individuals who are prone to have respiratory trouble postoperatively.

The technique of administration of the anesthetic, as well as the ability, training, and experience of the anesthetist, bears a definite relationship to the development of pulmonary complications (Rovenstine and Taylor, 80). A stormy anesthesia predisposes to pulmonary atelectasis (Christopher and Shaffer, 25), and a patient who continues to fight his anesthetic will have to fight for his convalescence (Eliason and McLaughlin, 37). These observations are in keeping with those of Van Allen, Lindskog, and Richter (97, 98), who report that "straining respiration," as in coughing, moaning, grunting, is necessary to produce atelectasis. Starr (90) states that hyperextension of the head by extending the occiput and lifting the point of the chin provides a more satisfactory airway than forcing the jaw forward. Aspiration

of secretions in the bronchial tree during anesthesia together with the use of the Trendelenburg position is likewise an important consideration in maintaining the patency of the air passages and preventing the entrance of material into them.

The importance of the depth and the duration of the anesthesia has already been referred to but they cannot be overstressed as pulmonary complications occur in direct relationship to them.

Cutler (33), who has long advocated the embolic theory of the development of pulmonary complications, observed that surgeons who were rough, allowed desiccation of the tissues, and took very little care of hemostasis experienced a higher percentage of complications than their more meticulous colleagues. Attention to detail here as in all other aspects of surgery is all important regardless of the theory adhered to.

If our concept of the relationship of wound pain, muscle spasm, and hypoventilation are acceptable it would seem plausible to assume that a large, widely traumatized, poorly closed incision in the upper abdomen would cause greater inhibition of breathing and coughing than would a smaller properly closed incision in the same region. Jones and McClure (58) believed that the use of the transverse incision in the upper abdomen resulted in a decrease in the number of postoperative pulmonary complications. Sloan (88), Singleton (87), and others have expressed a similar belief. Brock (16) states that the transverse incision which tends to close when the abdominal muscles contract is preferable to a longitudinal one which tends to pull open. No satisfactory statistical studies have been noted in the literature which confirm this impression. The midline supra-umbilical incision has proved very satisfactory from this viewpoint in Ogilvie's experience. Wound sepsis appears to be a significant factor in the development of postoperative pulmonary complications (King, 62). Capelle (22) believes that peritoneal irritation or inflammation results in only minimal degrees of inhibition of respiration and that the determining factor is voluntary and reflex spasm due to wound pain. He was able to minimize spasm by the use of a continuous injection of a local anesthetic into the wound and thus restore practically normal abdominal and thoracic excursion as well as vital capacity.

The abdominal dressing should be applied so that it gives adequate support to the wound but causes no impairment of tidal exchange (Beck, 7). Powers (79) found but slight reduction of the vital capacity when tight binders or adhesive strapping were applied. This averaged about 7.1 per cent, and, although he ascribed little significance to this change, it would seem that any further reduction of the already greatly impaired respiratory exchange would increase the incidence of pulmonary complications.

The position of the patient during the immediate postoperative period should be changed at frequent intervals (at least every hour), and the foot of the bed should be elevated to secure postural drainage of the lungs as well as to aid the return of blood to the right heart. Gray (45) suggests the use of the Trendelenburg position for the first twenty-four hours after operation in order to prevent aspiration of mucus or vomitus while the patient is abnormally quiet and before the cough reflex has returned. Burford and others prefer the lateral position which allows for better drainage and freedom for coughing and vomiting. Beck states that the head of the patient should be about a foot lower than his feet, and should be turned so that the mouth touches the sheet.

It is generally acknowledged that large doses of sedative or narcotics should be avoided both before and after the operation. These drugs, particularly morphine, depress the cough reflex and tidal exchange, as well as, the general activity of the patient. Many authors (Brock, 16; Haight, 47; Christopher and Shaffer, 25; Beck, 7) believe that small doses of morphine should be used to allay pain, and allow for effective coughing and hyperventilation, but emphasize that it should not be used in doses sufficient to depress the cough reflex. Capelle (22) was able to demonstrate an augmentation of the vital capacity amounting to from 3 to 5 per cent postoperatively after the administration of morphine.

The most satisfactory prophylactic measures are to encourage the patient to hyperventilate and cough effectively, and to change his position at least every hour. A great many articles regarding the merits of carbon dioxide administered routinely to induce hyperventilation of the lung have appeared in the literature. Beck (7) has listed 30 authors who favor its administration and 9 who could demonstrate no decreased morbidity following its use. Beecher (8) found essentially the same changes in the physiology of respiration whether carbon dioxide was used or not. Powers (79) demonstrated less fall in the vital capacity when carbon dioxide was used postoperatively. Henderson (90) states that in addition to increasing the volume of breathing by stimulating the respiratory center it induces increased tonus in the thoracic muscles, diaphragm, and to some degree in all the muscles of the body. Beck (7) concluded after a careful review of the literature

that hyperventilation of the lungs by use of carbon-dioxide inhalations should be continued as a routine measure. Holman (53), however, stated that he felt that voluntary hyperventilation would do as much good as carbon-dioxide inhalations.

Brock (16) has suggested that continued use of carbon-dioxide inhalations after operation might be harmful. He reasons that the forceful inspiratory efforts which the gas induces may serve to suck secretions even deeper into the lung. Also he points out that the administration of carbon dioxide may be most exhausting to the patient.

Most authors agree with Jackson's (56) contention that atropine should not be used to dry up secretions in the respiratory tract postoperatively because it tends to increase their viscosity and render their removal by cough more difficult. Instead, ammonium chloride or potassium iodide should be administered in small doses for their expectorant action.

It is important to encourage a certain amount of activity on the part of the patient to aid the return circulation and maintain tonus, but equally important is the forceful stressing of the necessity to hyperventilate, cough, and expectorate material in the bronchial tree. Brock (16) has said, "When the vice of immobility and the virtue of activity are pointed out to the patient, active co-operation usually follows."

### THE TREATMENT OF ATELECTASIS

Once atelectasis has developed all efforts should be made to evacuate the bronchial exudate and secure re-expansion of the collapsed area. This demands vigorous treatment which must be instituted promptly lest such complication as pneumonia, pulmonary abscess, or pulmonary gangrene develops. In the early stages of collapse the prognosis is very favorable if proper treatment is given.

The greatest factor in obtaining free expectoration is active effort on the part of the patient accompanied by changes in posture (Brock, 16). The lateral position with the foot of the bed elevated is the most effective position for securing drainage of the bronchial tree. Haight (47) has stated, however, that some patients cough more effectively in the semi-Fowler position and therefore, the position best suited to the patient should be employed.

Moore (71) has described a method of treatment which has been particularly effective in his experience. He applies a tight abdominal binder and places the patient in the lateral position with the involved lung uppermost and the foot of the bed elevated. The physician stands behind the patient and both he and the patient place one hand over the incision to give support to the abdominal wall. The patient is then urged to hyperventilate and cough. Vigorous percussion over the affected lung and carbon dioxide inhalations are used if evacuation is not satisfactory. He states that the patient will frequently volunteer the information that "That's all" when the bronchial tree has been emptied. Carbon-dioxide inhalations, steam inhalations, and ammonium chloride or potassium iodide should be used in conjunction with this therapy and the treatment may be repeated as indicated.

Haight (47) has reported successful results with intratracheal suction in postoperative atelectasis. The object of this procedure is to evacuate bronchial secretions when the cough remains wet and unproductive, either because the patient is unable or unwilling to co-operate. The method can be used interchangeably with bronchoscopic aspiration or can be used in preference as it is less strenuous on the patient and probably less traumatic. If necessary intratracheal suction may be repeated at intervals of from four to six hours.

Haight (47) recommends an ordinary No. 16 French soft rubber urethral catheter connected with a suction machine, preferably with an interrupter in the circuit. The catheter is introduced through the nares and into the larynx and trachea during the expiratory phase of cough or during the deep inspiration which follows it. By changing the position of the patient and manipulating the tube the different portions of the tracheobronchial tree can be cleared of secretions.

Although Elliott and Dingley (39) in 1914 suggested the use of artificial pneumothorax in the treatment of pulmonary collapse it was apparently not tried until Habliston (46) in 1928 reported satisfactory results in 2 cases of collapse, neither of which occurred postoperatively. Subsequently Moorman (72), Schindler and Gnagi (82), and Zukschwerdt and Lezius (106) have reported striking results with this method of treatment. The last authors believe artificial pneumothorax has not been given the recognition it deserves as in the 14 cases which they treated, cure resulted as if by magic.

They state that the pressure changes resulting from massive atelectasis bear chiefly on the delicate veins entering the right heart and produce a bending and kinking of these vessels. The unilateral low pressure draws blood away from the heart and causes a decreased venous outflow as well as a congestion of non-arterialized blood on the side of the collapse. Stasis and exudation into the alveoli then follow.

Pneumothorax is said to correct immediately many of these pressure alterations, place the diseased lung at rest, frequently dislodge the obstructing plug or plugs, and decrease the area of collapse and the volume of blood flowing through it (Schindler and Gnagi, 82). As a rule from 200 to 400 c.cm. of air are used, following which the patient begins to cough and expectorate. The dyspnea and sensation of oppression clear rapidly and the physical and x-ray signs of collapse soon disappear (Zukschwerdt and Lezius, 106).

Bronchoscopic aspiration in postoperative atelectasis was first reported by Jackson and Lee (57), and this method has been repeatedly used with gratifying results. Haight (47) states that this method of treatment is preferable to intratracheal suction when a single aspiration will probably be sufficient, when complete evacuation of the secretions is required, or when the application of adrenalin or cocaine to the edematous mucosa is indicated.

Zukschwerdt and Lezius (106) claim that this method of treatment is too risky and they prefer artificial pneumothorax. Others note that bronchoscopy should be resorted to only when all other methods of treatment fail, while some authors believe early bronchoscopic aspiration should be carried out especially when adequate facilities and personnel are available. Tucker (96) states that if the usual methods do not relieve the patient or if he is urgently dyspneic, bronchoscopy should be done. Immediate bronchoscopic aspiration is usually indicated when bilateral collapse is present.

Capelle (22) reports the use of novocaine anesthesia to relieve wound pain and spasm and facilitate both hyperventilation and cough. He believes this to be an effective prophylactic and therapeutic measure in postoperative atelectasis. The writer (44) has observed striking results from paravertebral anesthesia in the treatment of this condition.

Schwab (84) used a quinine and guaiacol preparation in the treatment of a series of 60 cases with pulmonary complications. He believed the quinine reduced the inflammation of the respiratory membranes and the guaiacol aided materially in the elimination of bronchial secretions. Moraldi (73) reported good results, both therapeutic and prophylactic, from a quinine and calcium preparation.

### THE TREATMENT OF POSTOPERATIVE PNEUMONIA

The treatment of postoperative, as well as primary, pneumonia has been much more promising since the advent of sulfapyridine. The prognosis is usually grave, however, because this condition is so often added to the troubles of an already seriously ill patient. The non-specific measures such as oxygen therapy, hyperventilation with carbon dioxide, and intravenous administration of fluids are to be instituted as indicated. The sputum should be typed promptly and specific serum administered when available. This may be given in conjunction with sulfapyridine as recommended in primary pneumonia. In any case, sulfapyridine should be started immediately once the diagnosis of pneumonia has been established.

Hinshaw and Moersch (52) report 21 cases of postoperative pneumonia treated with sulfapyridine with only 1 death. They usually give 1 gm. by mouth every four hours, day and night, but give double this amount for the first and frequently the second dose. No serious results attributable to the drug were noted. The oral route is the only one by which the drug can be given at present which necessarily limits its field of usefulness in postoperative patients to some extent.

Hinshaw (51) has worked out a set of rules to govern the use of sulfapyridine in his practice:

1. Adequate dosage is essential to treatment.
2. The dosage must be well distributed throughout the day and night.
3. The occurrence of nausea or even vomiting should not dissuade the physician from continuation of needed therapy.
4. Results are prompt. The drug may be abandoned if real benefit cannot be demonstrated on the chart within from forty-eight to seventy-two hours.
5. For the most part, sulfapyridine should be used only for patients who are seriously ill.

### SUMMARY AND CONCLUSIONS

The importance of postoperative hypoventilation as a predisposing cause of pulmonary complications seems well established. Hypoventilation appears to be due chiefly to pain and reflex spasm caused by a wound in the abdominal wall. Decreased tonus of the respiratory muscles, as well as other muscles, resulting from anesthesia, operative trauma, or narcosis, may also play a significant rôle. Bronchial secretions which may be increased or thickened by various factors are retained because the normal mechanisms for removal have been depressed. These mechanisms are cough, hyperventilation, ciliary action of the bronchial epithelium, and normal postural changes. The retained secretions frequently cause lobular or lobar obstruction, and the absorption of air from the blocked segment very soon results in atelectasis.

This condition can usually be avoided if proper prophylactic measures are carried out. These consist of active hyperventilation and cough on the part of the patient, frequent changes in position, and avoidance of excessive narcosis. Carbon-dioxide inhalations may assist in securing hyperventilation and effective coughing.

Bacteria contained in the secretions rapidly invade the collapsed segment and set up a pneumonia unless measures are promptly invoked to remove the obstructing mucus. The organisms usually present are derived from the upper respiratory passages, and are most frequently pneumococci.

The measures which have been found to be most effective in combating postoperative atelectasis are similar to the prophylactic measures, namely, cough, hyperventilation, postural drainage, frequent changes in position, and vigorous percussion over the affected lobe. In addition, intratracheal suction and bronchoscopic aspiration may be utilized if these measures fail. Artificial pneumothorax may be an effective therapeutic measure in massive atelectasis, but as yet has not been widely accepted. Likewise, the value of local anesthesia for relief of wound pain as an adjunct to more effective coughing and hyperventilation remains to be more completely studied.

If the diagnosis of pneumonia in the atelectatic lung is established, sulfapyridine therapy should be instituted immediately. It is probable that the use of this drug in properly selected and controlled cases will result in an appreciable decrease in the mortality from postoperative pneumonia.

Attention to detail during the pre-operative, operative, and postoperative periods should be our watchword in the care of the surgical patient, and only by this means can we expect to decrease the incidence and the mortality of postoperative pulmonary complications.

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# SURGICAL TECHNIQUE

## OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

**Maioli, M.: Evaluation of the Circulatory Efficiency in Surgical Practice** (La valutazione dell' efficienza circolatoria nella pratica chirurgica). *Clin. chir.*, 1940, 16: 51.

Maioli states that one of the principal factors in deciding on a surgical intervention is the evaluation of the resistance of the circulatory apparatus, because the operative traumatism subjects the heart and the vascular system to a strenuous test. Consequently, the surgeon will have to study the functional and anatomical condition of the heart and of the vessels and decide whether or not the probabilities are in favor of the patient's enduring the operation and whether or not the circulatory system should be prepared for the surgical traumatism in case of operation. The surgeon should rely on his own judgment based on numerous observations, and not on the judgment of the internist who attaches more importance to anatomical than to functional conditions, and is inclined to excess of optimism or pessimism.

The question of whether the circulatory system will be submitted to a strain by the intended intervention is easily answered. The selection of the anesthetic is motivated by the nature of the intervention and by the cardiac, hepatic, and renal condition of the patient. However, the question which directly involves the responsibility of the surgeon is what reaction the operation will cause in the circulatory system. Numerous tests have been proposed, but all are open to some objection. Therefore, the surgeon must consider the results of the various tests as objective data and use his clinical intuition analytically and synthetically to draw conclusions.

First, a careful examination of the circulatory apparatus of the patient at rest is indicated in all cases to establish the anatomical diagnosis. If the apparatus is found to be normal, the arterial pressure before and after some effort is determined, and possibly a test of the vagosympathetic equilibrium is made. If the apparatus is found to be seriously damaged, abstention from surgical intervention is indicated except in urgent cases. Intermediate cases require further study. The response of the apparatus to the orthostatic position and the behavior of the pulse after an effort in the erect posture must be observed. The time taken by the pulse to return to normal increases proportionately to the decrease in reserve power of the heart, and disturbances of the cardiac rhythm during the tachycardia are to be regarded as unfavorable signs. In this case, the behavior of the arterial pressure in the presence of an effort must be investigated.

As a general rule, it may be taken for granted that a patient having an arterial pressure of more than 150 mm. has hypertension and that one having a pressure of less than 120 mm. has hypotension. Hypertension, accompanied by marked arteriosclerosis and renal or myocardial lesions, contraindicates a serious operation. Hypotension facilitates the appearance of postoperative collapse, but its importance depends on its cause and the decision of the intervention must be subordinated to the latter. In the evaluation of the circulatory efficiency, the behavior of the arterial pressure under effort is valuable: the differential pressure increases in the normal subject, but it decreases when the effort exceeds the capacity of circulatory adaptation of the individual. Bad response, especially if associated with an unfavorable test of the pulse frequency, serves as warning that the surgical intervention may overtax the circulatory system and lead to disaster.

Another test is based on the volume of the heart in the presence of increased demands and requires the aid of roentgen examination; the effort, whether caused by exercise or the injection of adrenaline, produces passive dilatation in the miopragic heart. None of these tests has an absolute value; they reveal the degree of excitability of the heart and of tonicity of the vascular apparatus, as compared to normal: the excitability of the heart is very important for the evaluation of the circulatory efficiency, and one must know the anatomical diagnosis to determine the operative prognosis.

The circulatory apparatus may be prepared by a rest cure or by medication: digitalis and rest are indicated in functional disturbance based on slight reactivity of the heart to effort, especially in patients who are leading a strenuous life; digitalis will give poor or no results in case of manifest circulatory insufficiency in patients who have led a restful life. In some patients, a sedative and antithyroid treatment, associated with reconstituent therapy, is needed. Lability of the vasomotor tonus requires adrenaline and strychnine. Rebellious hyperthyroidism offers great danger for narcosis and intervention. The rhythm and the quantity of urinary elimination may constitute a good test of circulatory function, but are not of absolute value. Electrocardiographic examination belongs to the province of the specialist, and his conclusions are usually accepted without discussion. Nevertheless, the surgeon must base his judgment on clinical data collected personally so as to enable him to do without special investigations when they are unavailable, or to control them eventually.

RICHARD KEMEL, M.D.

**Van Nieuwenhuizen, C. L. C.: The Venous Blood Pressure After Performance of Work, a Functional Test of the Circulation** (Der venoese Blutdruck nach Arbeitsleistung, eine Funktionspruefung der Zirkulation). *Acta med. Scand.*, 1940, 103: 171.

The author proceeded from the fact, which has been known for a long time, that the venous blood

supply is a determining factor within very wide limits for the function of the heart and, also, that the body endeavors to maintain the venous blood pressure as long as possible until the blood reaches the heart. He, therefore, investigated the effect of bodily exertion upon the course of the venous blood pressure. For this purpose, two simple and daily applicable methods were combined, namely, the direct method of Moritz-Tabora for the determination of the venous blood pressure, and the method in which the bodily exertion is produced by the patient in the lying posture drawing up his legs fifteen times. This performance of work has the advantage that the zero point of the measurement of the blood pressure remains unchanged and that, furthermore, this work designates the same performance for every patient. After this exertion, the course of the venous blood pressure was followed for the duration of ten minutes (after 15 and 30 seconds, and after 1, 1½, 2, 2½, 3, 3½, 4, 4½, 5, 6, 7, 8, 9, and 10 minutes). In normal persons the venous blood pressure returned to the resting level as early as after fifteen seconds, to remain at this level, or to sink to a maximum of 15 mm. of water below the resting level in juvenile persons. This resting level lies between 30 and 90 mm. of water in normal persons. Other investigators obtained the same results in animal experiments and after the injection of greater amounts of fluid in normal persons. Variations from this course may, therefore, be considered as pathological.

The following investigations were made:

1. The venous blood pressure was taken after mechanical stasis before and after bodily exertion, and it was found that after bodily exertion the venous blood pressure showed a curve that was entirely above the resting value.

2. In cases of valvular diseases, in arterial hypertension, in auricular fibrillation, and also in valvular disturbances or the last combined with myocardial injury, in hyperthyroidism, and in "cor pulmonale" the venous blood pressure was determined before and after bodily exertion. The acquired curves may be divided into 4 types, in agreement with the severity of the symptoms and, therefore, they possess diagnostic significance. In addition, the curves give an insight into the mode of origin and the course of the decompensation.

Type 1. The venous blood pressure at rest is normal or somewhat above the normal. After performance of work there results a curve which fluctuates around the region of the resting level. This curve is found in healthy persons, but also in patients with a hypertension without decompensation and with auricular fibrillation and a sufficiently regular and low auricular frequency.

Type 2. The venous blood pressure is normal or lowered. After bodily exertion there results a lowering which lasts for ten minutes or even longer and the pressure is stronger than in normal persons. This course may be considered as an attempt at accommodation so as not to allow the terminal pressure in front of the right ventricle to rise with the aid of the depot. Such a curve denotes a beginning decompensation, which, because of the compensatory mechanism demonstrable on the basis of the investigations, has not yet led to the development of symptoms of stasis. Usually a "dyspnée d'effort" results.

Type 3. In spite of the compensation, the venous blood pressure has again risen in the resting state to a high normal or a somewhat higher level. Following exertion stasis results, which, after some time, usually from three to five minutes, is again compensated or overcompensated. The venous blood pressure then usually sinks markedly below the rising level. This type is usually associated with clinical signs of a decompensation, such as "dyspnée d'effort," swelling of the liver (depot function of the liver), nycturia, and sometimes a rapid pulse and slight edema.

Type 4. This type is found in pronounced cases of cardiac decompensation (dyspnea at rest, edemas, liver swelling, swollen jugular veins, a rapid pulse). The venous blood pressure is increased even in the resting state and a marked stasis appears after exertion which cannot or can barely be compensated for within ten minutes.

This course of the venous blood pressure after performance of work also shows clearly why determinations heretofore, which with few exceptions were always carried out in the resting state, were so unsatisfactory: with a distinct decompensation the venous blood pressure may still be normal (Types 1, 2, and 3). The various causes of cardiac decompensation showed, although they may easily be grouped in this classification, peculiarities specific for each type, which have been described. The determination of the venous blood pressure after performance of work is a simple and reliable method for the recognition of "decompensation of the heart." In addition it affords an insight into the nature of the origin and treatment of the circulatory disturbances in the venous system resulting from this decompensation.

LOUIS NEUWELT, M.D.

**Jones, R., Jr.: The Management of Old Contractures of the Hand Resulting from Third-Degree Burns.** *Surgery*, 1940, 7: 264.

Contractures of the hand and digits as a result of burns are common and these deformities often can be corrected by suitable operative measures, with subsequent improvement in the function of the hand. Each patient presents an individual problem and it is important to estimate the depth of the scar, its attachments, and the possible distortion of the deeper structures before the method of repair is chosen.

The patients fall into three groups. In the first are those with scars on the palmar surface of the digits and often on the palm which cause web-like flexion contractures of the fingers. These webs can often be released by the interposition of flaps formed by incisions made at an angle to an incision which is placed at the edge of the contracture and splits it.

The second group of patients present broad scars which are unattached to the deeper structures of the hand. These are best treated by excision of the scar, but a protective layer of fat should be left over the nerves and tendons. This defect is covered with a full-thickness graft on the palm, but a thick, split graft may be used if the dorsum of the hand is involved.

The third group of patients have a scar which extends from the skin to the muscles, tendons, or joints of the hand. This fibrous tissue should be stretched as far as possible pre-operatively by physiotherapy. After excision of the scar it is necessary that an adequate fat pad is interposed between the skin and deeper structures. For this method a previously prepared pedicle flap is usually necessary.

In the management of contractures proper physiotherapy and splinting with the use of elastic traction is of great assistance in obtaining return of function.

Photographs and illustrations demonstrating the type, treatment, and results of the various groups of contractures of the hand are shown.

HARVEY S. ALLEN, M.D.

**Levinson, S. O., Neuwelt, F., Necheles, H., and Others: Human Serum as a Blood Substitute in the Treatment of Hemorrhage and Shock.** *J. Am. M. Ass.*, 1940, 114: 455.

In the treatment of hemorrhage and shock, transfusion with whole blood is desirable, but the securing, matching, and the performance of the Kahn and similar tests entail considerable unavoidable delay. Human serum, on the other hand, may be collected at leisure, stored for an indefinite period, and used immediately when a situation demands, without cross-matching or fear of any reaction. Loss of erythrocytes is seldom a vital factor in severe hemorrhage. The sudden and marked diminution in the circulating blood volume is of grave significance, however, because this oligemia leads to rapid development of secondary shock.

Experiments were performed on dogs anesthetized with pentobarbital sodium, in which the blood pressure was recorded in the usual way. A femoral artery was prepared for bleeding and a femoral vein for infusions. After a control blood pressure had been recorded, the animal was bled rapidly until its blood pressure fell to shock level (systolic pressure from 40 to 60 mm. of mercury). The blood pressure was maintained at shock level for from ten to twenty minutes before an infusion of either saline solution or dog serum was given. The amount of fluid administered varied from one-fourth to several times the amount of blood removed. Such experiments demonstrated that immediate infusion with saline solution produces a moderate degree of recovery, which, however, is less marked than that following serum infusion. Delay in administering fluids, on the other hand, caused a loss of effectiveness of the saline solution, the influence of which on blood pressure was only temporary, in contrast with the sustained effect of serum.

Somewhat similar experiments were done, in which a state of post-hemorrhage shock was brought on by a single massive hemorrhage. The animals were left in this condition for two hours so that increased capillary permeability and secondary shock might develop. The animals were then transfused with various fluids. It was found that some recovered to a varying degree in the two-hour period, while others remained in shock, and therefore transfusions with saline solution, serum, or blood gave varying and inconsistent results. It is worth noting that those dogs having the highest blood pressure at the conclusion of the experiment had received either blood or serum. Another interesting feature was that the blood proteins remained at normal levels following the serum infusions, whereas they showed considerable diminution after saline infusion. Experiments with long-continued graded bleedings also demonstrated the superiority of serum over saline solution.

Hoitink has shown that the immediate infusion of large quantities of normal saline solution in primary shock is as beneficial in saving the lives of dogs as any other blood substitute. In secondary shock, however, saline solution is no longer a life-saving fluid because of the increased capillary permeability.

The authors conclude that serum overcomes all the effects of hemorrhage in dogs except the loss of red cells. They anticipate the extensive use of human serum in war surgery. AUGUST JONAS, JR., M.D.

**Strumia, M. M., Wagner, J. A., and Monaghan, J. F.: The Treatment of Secondary Shock.** *J. Am. M. Ass.*, 1940, 114: 1337.

Shock is the result of a decrease in the volume of circulating blood. The ideal therapeutic agent to combat this condition is one which brings about a rapid and permanent increase in the blood volume. Whole-blood transfusions, gum acacia, and intravenous infusions of sodium chloride and dextrose solutions have been used clinically to combat shock, but these measures are often inadequate and may even be dangerous. Experimentally, lyophile serum and plasma has been used successfully to overcome shock. Strumia and his coworkers believe that citrated plasma has many advantages over other agents in the treatment of shock. They have used it successfully in a number of clinical cases, 10 of which are presented and discussed in detail.

The plasma should be prepared in the following manner:

Proportionally, 500 c.cm. of blood are mixed with 100 c.cm. of a solution containing 2 per cent sodium citrate in physiological normal saline solution. The mixture is centrifuged and the plasma separated by suction. The plasma may be used fresh or stored at 4° C. after the addition of 1:10,000 merthiolate solution. No cross matching is necessary, but each batch is tested serologically. At the Bryn Mawr Hospital, where this report originated, plasma is collected as a by-product at the end of five days from stored whole blood. Plasma may be preserved

for long periods of time by drying from the frozen state, the so-called "lyophile" or "cryochem" process.

According to the authors, plasma has distinct advantages over other shock combating agents. These advantages are:

1. Over crystaloids. Plasma does not leave the blood stream as do the crystaloids (saline and dextrose).

2. Over gum acacia. It does not produce severe and even fatal reactions.

3. Over serum. Plasma has a greater yield and does not cause reactions.

4. Over whole blood. No typing or cross matching is necessary. Plasma is free from reactions and very large and repeated doses may be given. Plasma can be kept much longer than whole blood, and it can be transported without affecting it in any way. Plasma does not add to the concentration of erythrocytes, a decided advantage in severe burn cases. Plasma is always ready to be used for an emergency, and a plasma bank is considerably simpler to operate than a blood bank.

Finally, the authors point out that plasma is an ideal agent for the treatment of shock under war conditions. LUTHER H. WOLFF, M.D.

**Hall, C. C.: Aspiration Pneumonitis: An Obstetrical Hazard.** *J. Am. M. Ass.*, 1940, 114: 728.

The writer reports a case, in October, 1937, of aspiration pneumonitis occurring in a primipara, thirty-three years old, at full term. The patient entered the hospital at 1:30 A.M. in the first stage of labor. She was given a mixture of scopolamine, morphine, and cactine (H.M.C. 1) at 3:00 A.M. so that she could secure some sleep. The following forenoon the labor pains were weak and irregular. Rectal examination showed only 1 cm. of dilatation. At 2:00 P.M. she was given further medication consisting of sodium barbiturate (7½ gr. by mouth) and scopolamine (1/150 gr. by hypodermic). At 2:15 P.M. 2 minims of solution of extract from the posterior lobe of the pituitary gland were given hypodermically. This gave regular, strong contractions. The patient became noisy and excitable and was given ⅛ gr. morphine.

Dilatation was complete by 6:30 P.M. She was taken to the delivery room and under gas anesthesia it was decided to deliver the head with low forceps. Four minutes after beginning gas anesthesia the patient gagged and vomited. Respiration ceased and she became very cyanotic. Artificial respiration was resorted to and she soon resumed breathing. Her color returned and remained good and there was no coughing. The baby was delivered in good condition. The mother was returned to bed with a pulse rate of 84 and respiration of 26.

By 9:30 P.M. the patient was cyanotic and gasping for air. Examination of the chest showed coarse bubbling râles throughout. Atropine 1/150 gr. was given and inhalations of oxygen and carbon dioxide were started. Four hundred c.cm. of 25 per cent sucrose were given intravenously and the atropine dosage was repeated. The patient was placed in an oxygen tent and 1 ampoule of metrazol was ordered every four hours.

An x-ray study of the chest made the following day revealed very extensive coarse mottling extending throughout the right lung, most pronounced adjacent to the hilus, and gradually diminishing toward the periphery of the chest. Large, soft indistinct densities appeared as shadowing, more evident in the middle lobe of the lung. In the left lung there appeared a similar but not quite so extensive a mottling involving chiefly the lower portion of the lower lobe. Leucocyte counts varied from 17,200 to 27,900. In the oxygen tent the respiration rate remained high between 40 and 50 per minute with a pulse rate varying from 110 to 140. The temperature averaged only about 100° F. The patient coughed rarely and then raised small amounts of thick rusty sputum. Stained smears revealed a streptococcus to be present.

There was but little change in the clinical condition during the time the patient lived. Repeated x-ray examinations of the chest made on four occasions showed a progressive increase in the areas of density. The patient received two blood transfusions of 500 c.cm. each. Death occurred on the thirteenth day after delivery and autopsy revealed both lungs to be the site of diffuse moist consolidation, with air present only in the extreme apices of the lungs.

The writer was able to collect histories of 14 other similar cases occurring in the practice of colleagues in nearby cities. Apparently aspiration pneumonitis is not a rare condition as 12 instances occurred within the last two years. It is a most serious complication of labor. Among the 15 cases there were 5 deaths, and the remaining cases required prolonged hospitalization.

Aspiration pneumonitis may be divided into two distinct types; that in which the aspirated material is of a solid nature and that in which it is fluid. In the first, death may occur rapidly from the mechanical obstruction of the air passage. When the aspirated material is fluid in nature there results, apparently, a chemical pneumonitis. The x-ray picture may resemble that of bronchopneumonia but there are clinical differences. The author believes that the reaction in the lung tissue results from certain fractions of the gastric juice itself.

The question arises as to whether the type and amount of premedication and the gas analgesia used during labor have any effect on this condition. The author does not believe that the blame for aspiration pneumonitis can be placed on the anesthetist. A valuable suggestion as regards prevention of this complication may be that the patient abstain from all solid food during labor. Every delivery room should be equipped with an efficient suction apparatus. Possibly the anesthetist should not be permitted to fasten the gas mask on the patient's head. JOHN W. NUZUM, M.D.

**Zucchi, C. A.: Clinical Considerations on the Cases of Pulmonary Embolism Observed in the Rizzoli Institute during the Decade 1929 to 1938** (Considerazioni cliniche sui casi di embolia polmonare osservati all' Istituto Rizzoli nel decennio 1929–1938). *Chir. d. organi di movimento*, 1939, 25: 153.

Zucchi found that death due to embolism of the pulmonary artery occurred in 14 cases at the Rizzoli Institute during the past ten years: this represented 9.08 per cent of all the deaths. Eleven of the patients were admitted with a traumatism of the lower extremities, and 1 each with deforming arthritis, rhizomelic spondylosis, and congenital dislocation of the patella.

Embolism may occur at any age, but is observed especially after the age of fifty years; in the present cases, the ages ranged from seventeen to seventy-two years, with the highest frequency between fifty-six and sixty-five. There were 12 men and 2 women; this proportion is the inverse of that generally reported and is probably due to the fact that the cases were mostly traumatic. Opinions on the influence of the seasons differ: November and December showed the greatest frequency of occurrence in the present series. The clinical histories revealed that the embolism occurred from four to twenty days after the traumatism or the intervention, and with major frequency about the fifteenth day; this corresponded to the number of days needed for the return of the cardiac activity, which is the principal cause of the mobilization of the thrombus, while the reduced cardiac activity of the first days favors the formation of the thrombus. The symptoms of embolism appeared suddenly in most cases and developed in from five minutes to eight hours; they were preceded by clinically demonstrable thrombosis in 2 cases and by pulmonary infarct in another 2 cases.

The diagnosis was made from the sudden appearance of marked dyspnea; a feeling of precordial anxiety; pallor with cyanosis of the mucosa; marked variations in the frequency, strength, and rhythm of the pulse, associated with nausea, vomiting, urgency of defecation and urination; and marked perspiration. In addition, the absence of heart disease and the execution of an effort or a movement shortly before the occurrence of the embolism were taken into consideration: an effort, however slight, is sufficient to dislodge a thrombus.

In death from embolism the sudden suspension of the circulation to the lungs is not the only factor to be considered. Necropsy showed in 1 case a small embolism in one of the branches of the pulmonary artery of the left lobe, and, undoubtedly, death was due to a reflex spasm of the entire pulmonary system caused by the presence of this small embolism. In case of preceding pulmonary infarct, death may be caused by the mobilization of new thrombi. In 1 of the patients who did not show cyanosis, an electrocardiogram was taken to clear up the diagnosis; it presented a lowering of the Q wave in the third lead, combined with a heightening of the ST wave in the same lead, and a nodule in the descending R line in the second and third leads.

The treatment consisted of cardiokinetic drugs, oxygen, and venesection. Surgical intervention has been performed successfully by some authors. Various prophylactic measures have been recommended, but few have been of any use. The most reasonable ones seem to be: abstention from surgical intervention in the old and the obese, pre-operative and post-operative treatment of slight cardiac decompensation; pre-operative removal of varicose veins; early reduction and immobilization of fractures; the administration of sympathol (vasoconstrictor); ligation of thrombosed veins; and removal of a thrombus. At the first signs of embolism 0.06 gm. of eupaverin should be given intravenously and the dose repeated soon if the first injection remains without effect. Morphine, immobilization, and, if possible, embolectomy are indicated. RICHARD KEMEL, M.D.

**Bergquist, G.: Postoperative Thromboses. Preliminary Report** (Ueber postoperative Thrombosen. Vorlaeufige Mitteilung). *Acta chir. Scand.*, 1940, 83: 415.

Bergquist's preliminary communication reviews the literature on postoperative thromboses. The present concept is that thromboses and embolism after operations are due probably to changes in the blood flow of the legs, to biochemical changes of the blood, and perhaps to damage of the endothelium. The author agrees with these views, but stresses postoperative changes in the blood flow ("whirlpool formation") causing a prethrombotic condition, which when persisting for some time leads to thrombosis because of changes in the composition of the blood and an increased tendency to coagulate.

The anticoagulant heparin has been used for a number of years by many authors in attempts to prevent postoperative thromboses. In order to find definite indications for the use of such an anticoagulant as a preventative, Bergquist studied the course of the coagulation time and the number of thrombocytes after operation. While the number of thrombocytes showed no important changes after operation, the coagulation time had a tendency to fall regularly after operation from the fifth to the eighth day, occasionally also to the tenth day.

Bergquist used Petrén's method for determination of the coagulation time. A survey of all postoperative thromboses which occurred from 1929 to 1938 in his hospital showed that most of them happened around the same time postoperatively, or possibly somewhat later, i.e., from the sixth to the tenth day after operation.

Assuming that shortened coagulation time together with other factors (whirlpool formation) is a prerequisite for thrombus formation, Bergquist instituted heparin prophylaxis in cases in which the coagulation tests showed less than three minutes. Out of a test group of 4 such patients, 2 received heparin and remained thrombosis-free, and 2 received only the customary postoperative care. These

2 developed thrombosis and 1 of them died from pulmonary embolism.

Bergquist gives heparin according to the following schedule:

As soon as the coagulation time falls below three minutes (according to a more recent experience—as soon as the coagulation time diminution is more than one minute from the pre-operative value), 0.6 c.cm. of a 5 per cent solution of heparin are given intravenously. If the coagulation time after four hours still is subnormal, 1 c.cm. is given, and followed by another check-up after six hours. If the result still is unsatisfactory, 2 c.cm. are given, and a test is made seven or eight hours later. No further administration has been found necessary.

Of the 50 patients studied for a determination of the coagulation time, 8 showed values low enough to warrant the institution of heparin prophylaxis. They were given heparin, and no thrombosis occurred in any of them nor in any of the 42 other patients.

Bergquist has found that estimation of the coagulation time according to Petrén can be done advantageously from finger blood. If heparin cannot be given intravenously, it should be injected intramuscularly, but larger doses are required if this route is chosen. HEINRICH LAMM, M.D.

## ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

**Bordonaro, F.: Clinical Contribution to Conservative War Surgery** (Contributo clinico alla chirurgia conservativa di guerra). *Chir. d. organi di movimento*, 1939, 25: 189.

Bordonaro states that great advances have been made in conservative surgery of the most varied and grave lesions caused by firearms, because of the use of Loehr's method of treatment, which limits surgical intervention to a minimum and thereby facilitates the surgical service of the combat line. Loehr first employed his treatment in cases of acute osteomyelitis in which he made a simple incision of the soft tissues and of the periosteum and applied cod-liver oil and a plaster cast. The good results which he reported led to the use of the method in chronic osteomyelitis and in cases of other septic processes and of recent wounds with marked loss of tissue; the great rapidity and intensity of the processes of epithelization and granulation were attributed to the presence of Vitamins A and D in the cod-liver oil.

During the late Spanish War, the method was used extensively and showed that it was possible to save extremities with enormous lesions which previously imposed immediate amputation. It allowed rapid systematization of the most serious wounds and elimination of gauze and rubber drainage in most cases, as it necessitated only a window in the plaster cast to ensure the outflow of exudates. It could be applied during the first hours after the injury was received and constituted the best expectant biological medication for the conservative surgical treatment of the extremities. The biological and biochemical phenomena produced in the tissues by cod-liver oil create the possibility of reducing to a minimum the traumatism of initial surgical intervention on the foci of fracture and on the tissues; there is no necessity for inflicting a long and careful preparation of the wound on a patient who is already in a state of shock. The early appearance of the repair processes provides an efficient protection against secondary infection of the wound and helps in overcoming primary infection.

In the secondary treatment of open fractures of war, the method has an undeniable effect on septic complications and especially on acute and chronic osteomyelitis of the fragments. It has been proved that the combination of the treatment with cod-liver oil, immobilization in the plaster cast, and continuous skeletal traction by means of a metallic wire provides ideal results. In spite of the complication, the course is subfebrile, and does not necessitate any surgical intervention, except for some incision of the soft tissues to give an outlet to the pus formed in the osteomyelitic foci. In addition, it is possible to obtain delimitation and complete spontaneous elimination of sequestra, before cicatrization of the lesions and consolidation of the fractures, in spite of the marked loss of bony substance and the long period of suppuration. A whole series of factors which would derive from the systematic use of the method make it of immediate interest to the military sanitary service during war; these factors are the ideal immobilization of fractured extremities for the transportation of the wounded, the uniformity of the treatment of open fractures passing through the collecting stations, and the simplification of the sanitary service of evacuation. In addition, the method saves the wounded from serious and prolonged sufferings due to the usual methods of early surgical treatment, beginning at the front line.

RICHARD KEMEL, M.D.

**Howes, E. L.: The Immediate Strength of the Sutured Wound.** *Surgery*, 1940, 7: 24.

Wetting of catgut or silk sutures causes them to lose about 30 per cent of their dry-thread strengths. Knotting causes a loss of from 40 to 50 per cent, while wetting and knotting together cause a loss of from 50 to 60 per cent of the dry-thread strength. This "functionating strength" is not, however, always proportional to the dry-thread strength. Number 2 or 3 catgut does not have a greater functionating strength than that of No. 1, and the comparative functionating strengths of different sizes of silk have a much smaller range than their dry-thread strengths.

The holding powers of various soft tissues were tested in a tensile strength machine. The only tissue which had a holding power greater than that of the functionating strength of No. 00 catgut or silk was fascia, and that only if the pull was directed perpendicularly to its tissue fibers. In that case it took No. 1 catgut to be stronger than the fascia.

The increase in wound strength resulting from the use of multiple sutures was studied by means of a sutured abdominal wall of a rabbit, in which the stitches were placed 1 cm. deep. The holding power of the tissue increased, although not proportionally, up to the maximum when the sutures were 0.5 cm. apart. The functionating strength of the suture material increased, however, in direct proportion to the number of stitches placed. The ratio, then, of functionating strength to holding power increases so that the greater the number of stitches the smaller the size of the suture material needed.

Experiments on suturing the skin of the dog showed that a continuous suture was no stronger than an interrupted suture line with the same number of bites. The former is obviously more risky, because if one strand breaks all is gone. Larger bites of fascia give slightly more strength than small bites, but this advantage is probably offset by more necrosis of tissue and more suture material in the wound.

The author concludes that: there is no need of suture of any other tissue but fascia except to eliminate dead space or, in the case of the peritoneum, to prevent herniation; when multiple sutures are used there is no need of using a suture stronger than No. 0 catgut; increasing the number of sutures increases the holding power and provides a better ratio of functionating strength to holding power; better healing is usually obtained when deep bites are not used; placing sutures in fascia so that they will pull parallel to the fibers should be avoided by special construction of the wound, or else mattress sutures should be used; and interrupted sutures should be recommended as preferable to continuous sutures.

RICHARD WARREN, M.D.

**Rocchi, F.: Research on the Pathogenesis of Tetanus by Parabiosis** (Ricerche sulla patogenesi del tetano mediante la parabiosi). *Policlin.*, Rome, 1940, 47: sez. med. 33.

In order to study the perfusion of tetanus toxin throughout the organism, the author injected it into several pairs of rats which had been previously united in parabiosis by the method of Morpugo. Four experiments were designed to differentiate the lymphatic, hematogenous, and neural routes through which the toxin might be conveyed.

In the first experiment, after 2 normal rats had been united in parabiosis for fifteen days, two lethal doses of toxin were injected into the right thigh of the right animal. In twenty-four hours the injected extremity became rigid in extension and after thirty-five hours the animal assumed a definite homolateral pleurothotonus. The other animal assumed an attitude of emprosthotonus. The animals were separated at this time and the one injected in the thigh soon died with local tetanus and pleurothotonus. The other animal slowly recovered, losing the tetanic attitude.

In the second experiment, the sciatic nerve in a parabiotic animal was isolated and injected with one lethal dose of toxin. After two hours the adjacent 15 mm. of the nerve were excised and the wound was closed. In eighteen hours the animal developed tetanus of some of the thigh muscles and some homolateral pleurothotonus. The other animal later developed emprosthotonus.

The third experiment was conducted upon 2 parabiotic rats in which the distal end of the left rat's sciatic nerve had been anastomosed to the proximal end of the nerve of the other animal. Twenty days after the anastomosis, all cutaneous and muscular connections were severed and the left rat was given 50 lethal doses of toxin in the leg. The only bridge between them was the nerve, which was kept moist with saline. In eight hours, the right rat died with a syndrome of general intoxication. The nerve was immediately severed and a 1 cm. segment of it was macerated and injected into a third rat which died in from thirty-six to forty-eight hours with tetanus on the side injected. The left rat died in thirty-six hours with tetanus in pleurothotonus.

The fourth experiment was concerned with chronaximetric determinations before and after the injection of tetanus toxin.

The following conclusions are formulated:

1. Tetanus effected by a route rigorously hematogenous is characterized by sustained contractions with the flexors predominating over the extensors, namely, emprosthotonus. However, subcutaneous or intramuscular injection of toxin is followed by classical local tetanus with multiple contractions. It is demonstrated that the same toxin can be made to yield the predicted types of tetanus as an exclusive function of the diverse routes of absorption.

2. In 2 parabiotic animals, the local tetanic attitude assumed in the 1 injected with the toxin is dependent upon the greater amount of tetanogenesis prevalent in the inoculated side.

3. The absorption of toxin through a nerve trunk occurs along the axis cylinders with localization in the corresponding nerve centers and also through the endoneural lymphatics with secondary hematogenous diffusion throughout the organism.

4. The so-called local tetanus is the result of accumulations in the corresponding nerve centers of two charges of toxin, one arriving via the axis cylinders and the other arriving via the lymphohematogenous route. Animals that apparently have tetanus of small muscle groups really have hypertonic tetanus which is clinically not apparent but which is demonstrable by chronaximetric studies in remote muscle groups. FRANK MCDOWELL, M.D.

**Whittingham, H. E.: Anaphylaxis Following the Administration of Tetanus Toxoid.** *Brit. M. J.*, 1940, 1: 292.

The prophylactic inoculation of man against tetanus was until recent years performed by giving a subcutaneous or intramuscular injection of tetanus antitoxin soon after the receipt of an injury or during the incubation period of the disease. The main drawbacks to this type of prophylaxis are that the immunity given is only passive, partial, and temporary,

lasting merely a few weeks, and that serum sickness is a common occurrence.

To overcome these defects tetanus toxoid was developed, and it was used on a large scale from 1936 to 1938 by the British Army. This material apparently has the power to produce an active and relatively permanent type of immunity to tetanus, and it can be accepted as proved that for two years (some investigators say five years) after immunization with tetanus toxoid the antitoxin content of the blood can be relied upon either to prevent the occurrence of tetanus or so to modify the infection as to guarantee cure with modern anti-tetanus therapy. Two doses of 1 cm. are given subcutaneously at an interval of not less than six weeks.

The author describes 2 cases of anaphylactic shock following the administration of a second dose of tetanus toxoid, and reviews the incidence of general and local reactions following the subcutaneous inoculation of 61,042 healthy individuals. Acute reactions occurred in 2 cases (0.003 per cent), less severe constitutional symptoms in 12 cases (0.02 per cent), and local reactions in 651 cases (1.06 per cent). Although the incidence of general reaction is rare it is advisable to be prepared to treat it expeditiously with adrenaline when it does occur. JACOB M. MORA, M.D.

**Firor, W. M., Lamont, A., and Shumacker, H. B.: Studies on the Cause of Death in Tetanus.** *Ann. Surg.*, 1940, 111: 246.

In an exhaustive series of animal experiments, the authors found that the injection of as little as 1/400 of a lethal dose of tetanus antitoxin placed in a non-vital area of the central nervous system (the lumbar cord of a dog) caused death. The injection of less than a lethal dose of toxin into organs other than the central nervous system is never fatal.

Studies of the metabolic changes consequent to the constant muscular spasms revealed no changes which would account for death. In the absence of muscular spasms life is prolonged to some extent. However, those animals receiving relatively small doses of toxin have a far longer period of violent convulsions and survive longer than those animals receiving relatively large doses.

All of these facts led to the conclusion that the lethal agent must be carried from the point of injection of the toxin in the lumbar cord to some vital center. The lethal agent does not travel up the cord, because by transecting and by ligating the injected cord it was shown that the lethal agent did not pass up the spinal canal in the cerebrospinal fluid or within the substance of the cord itself.

Death cannot be attributed to a multiplication of the tetanus antitoxin molecule. This possibility was thoroughly explored and no experiments showed such an occurrence. General signs of tetanus, such as trismus, opisthotonos, and muscular rigidity never appear in animals dying from an injection of toxin into the cord. Finally, death occurs even though the blood and lymph contain large amounts of anti-tetanic serum throughout the entire course of the experiment. Obviously, if the toxin were multiplied and absorbed into the blood stream, it would be neutralized by the antitoxin.

These five essential facts led the authors to suggest that tetanus toxin in the spinal cord is altered into or liberates a different lethal agent, which is absorbed by the blood stream and is carried to some vital center where it produces its lethal effect.

Further experimental evidence is presented supporting this suggestion, which has been made by previous workers, viz., Courmont and Doyen, Pohl, Zupnik, and Zuger and Friedmann. Alteration of the toxin such as described would explain the experimental results of Abel and Chalian, who showed that after the intravenous injection of one or more lethal doses of tetanus toxin, the administration of even large amounts of anti-tetanic serum failed to save life if before the serum was given the animal had clearly evident symptoms of a descending tetanus and had fixed in his tissues one or more lethal doses of the toxin. They showed further that even though the animal's tissues had fixed many lethal doses of toxin, the anti-tetanic serum could save life if given not later than at a certain stage of the incubation period, before the appearance of symptoms of general tetanus. This would also explain the puzzling clinical finding that the use of tetanus antitoxin has not appreciably lowered the mortality rate of those patients who did not receive antitoxin until after the appearance of the central-nervous-system symptoms of tetanus.

It then appears likely from animal cross-circulation experiments and others that the lethal agent is not neutralized by tetanus antitoxin, and that the lethal agent may act chiefly on the respiratory center. For this reason the lethal action of this new substance may be enhanced by respiratory depressants. It appears that the use of respiratory-depressant drugs in cases of human tetanus should be undertaken with extreme caution. Probably respiratory stimulants and artificial respiration will prove of value.

It is emphasized that this experimental work so far reported should by no means be interpreted as making unnecessary the use of tetanus antitoxin as a therapeutic agent in clinical tetanus. Since in human beings there is no way of telling whether a lethal dose has been fixed, the clinician should continue to use antitoxin in local or central tetanus in the hope that a lethal dose has not yet been fixed by the body tissues. JOHN E. KIRKPATRICK, M.D.

**Ritossa, P.: A Report on Serum Therapy of the Malignant Pustule of Anthrax** (Contributo alla sieroterapia del carbonchio). *Settimana med.*, 1939, 27: 1327.

The author reviews the history of anthrax and its treatment, and presents a series of cases seen in the Clinic of Infectious Diseases of the University of Rome. This series represents a period beginning with March, 1936, and concluding with September, 1939. All cases were treated exclusively with serum,

and are offered for this reason, as being helpful in the evaluation of the ultimate place of serum in the management of anthrax. The highest incidence of infection was found to exist in rural communities, among male adults, facts easily explained by the occupational character of the disease. For the most part, the mode of transmission was by direct contact with infected animals, either as herder or butcher, although isolated cases seemed to be traceable to fly-bites, penetrating wounds from infected instruments, or the domestic handling of infected meat. It follows that all cases presented the primary cutaneous form, either pustule or malignant edema, and no case of pulmonary or intestinal anthrax came under observation, although in a small number of cases the infection spread and septicemia resulted, as proved by positive blood cultures. In all but 6 cases the lesion occurred singly, most frequently on the head, neck, and upper extremities. All cases were proved, not only by the clinical characteristics but by the bacteriology.

Treatment was begun in 2 cases on the first day, in 12 cases on the second day, in 32 cases on the third day, in 12 cases on the fourth day, in 12 on the fifth day, and in the remaining cases at a later time. For the most part the serum was given by intramuscular injection, the intravenous route being reserved for those cases in which septicemia was present or for those which appeared to be in serious condition. The amount of serum varied from 100 to 200 c.cm. daily, according to the gravity of the case. Duration of the treatment generally varied also from three to six days, the average total dose being from 500 to 800 c. cm.

No disturbances were noted other than serum sickness, which occurred in 32 of the 90 cases constituting the series and was manifested chiefly by urticarial or morbilliform eruptions, without elevation of temperature. The beneficial results of the serum therapy were observed from the second day on, and the local lesion was seen to diminish rapidly along with the constitutional signs and symptoms, the temperature returning to normal from the second to the sixth day. The mortality for this series was 7.7 per cent. One of the 7 patients died several hours after admission; 3 others entered with positive blood cultures from the fourth to the sixth day, while the remainder showed concomitant pre-existing disease of a serious nature.

The results of serum therapy were therefore summarized as follows: in 1 case, adequate amounts of serum were not able to prevent the development of septicemia; in 3 other cases in which septicemia was already present, generous amounts of serum administered intravenously were not sufficient to prevent a fatality. It was therefore concluded that the local lesion should be treated only by warm moist sterile dressings and by the liberal administration of serum, and that septicemia, once it has set in, is difficult to cure, even with large amounts of serum administered intravenously.

EDITH FARNSWORTH, M.D.

**Stephenson, D., and Ross, H. E.: Chemotherapy of Clostridium-Welchii-Type-A and Clostridium-Septique Infections in Mice.** *Brit. M. J.*, 1940, 1: 471.

Sulfanilamide and sulfapyridine were found to protect mice against a small number of lethal doses of clostridium welchii Type A injected intraperitoneally as suspensions of vegetative organisms in sterile soil suspension. Treatment with anti-toxic serum was effective in the case of a strain of high toxigenicity, but was ineffective against a strain of low toxigenicity but of probably higher invasiveness. When the infected soil suspensions were injected intramuscularly, considerably more organisms were necessary to produce a fatal result. The drugs were of value only against sublethal infections. Serum treatment was better, and saved mice even from lethal doses.

*Clostridium septique.* Sulfanilamide had little influence on infections of mice produced by the intraperitoneal or intramuscular injection of suspensions of sporing and non-sporing organisms in calcium-chloride solution or sterile soil suspension. Sulfapyridine was found to be better. Given in large doses, it saved 50 per cent of the animals. Treatment with a single dose of anti-toxic serum was at least as effective as sulfapyridine, but the best results were obtained when sulfapyridine was combined with serum. Large doses of the drug were given immediately after infection, and serum was given up to twenty-four hours later.

By tests made with these two strains of clostridium oedematiens, it has been shown that neither sulfanilamide nor sulfapyridine has any influence on the course of the infection. SAMUEL KAHN, M.D.

**Leriche, R.: The Treatment of Infections by the Intra-Arterial Route** (A propos de la thérapeutique des infections par voie intra-artérielle). *Mém. l'Acad. de chir.*, Par., 1940, 66: 47.

Leriche has employed intra-arterial injections since 1929 and has found this procedure one of the most effective methods of treating certain localized surgical infections. The intra-arterial injection of an antiseptic brings it most rapidly and most directly to the infected tissues; its effect may be enhanced by blocking the circulation temporarily below this point.

The author has employed various antiseptics for intra-arterial injection, but has found mercurochrome to be the most effective; when this drug is given intravenously it may have certain undesirable effects, but he has never seen the slightest ill effect when it is given intra-arterially, even if injections are repeated daily for a week or two. Recently he has used soluseptazine (a sulfanilamide compound), in some cases with equally good, but not superior, results.

Intra-arterial injections of mercurochrome have been employed in cases of suppurative arthritis, in complicated fractures, in diffuse phlegmon, in lymphangitis, and in infected gangrene. The injec-

tions have been combined with such surgical procedures as are indicated to establish drainage and remove diseased tissue. Intra-arterial injections may also be used in cases of trauma, when there is infection or danger of infection of the wound. However, this does not make it possible to dispense with proper surgical treatment of the wound—excision of injured tissue and drainage. The method might well be employed in war wounds.

Leriche has also employed scurocaine by intra-arterial injection in the treatment of the pain of gangrene. Not only does scurocaine so administered have an anesthetic action, but it also has a vasomotor action, producing dilatation of the smaller blood vessels and hyperemia of the tissues with resulting local leucocytosis and other changes that aid in combating infection. The author's observation of the effect of the antiseptic solution injected intra-arterially leads him to conclude that these drugs may have, in addition to their direct antiseptic action, a vasomotor action which increases the resistance of the tissues to infection.

ALICE M. MEYERS.

**Fuller, A. T., and James, G. V.: Dosage of Sulfanilamide in the Prophylaxis of Wound Infections.** *Lancet*, 1940, 238: 487.

The effects were compared, in man, of plain sulfanilamide (shellac coated, collodion coated, and keratin-coated tablets, and proseptasine) as regards concentration of sulfanilamide in the blood after the administration of doses of 1.5 gm. in the different types of tablets. Also compared were the percentage excretion, and the rates of excretion of sulfanilamide after different tablets, and their efficiency was expressed by dividing the concentration of sulfanilamide in the blood at any given time by the rate of excretion at that time. Other studies included a comparison of the concentrations of sulfanilamide in the blood after a single 1.5 gm. dose given in intact tablets and in solution. The blood concentration levels after 1 gm. of sulfanilamide every eight hours and after treatment with the recommended dosage were recorded.

The results obtained supported in the main recommendations made by the War Office for the prophylactic use of sulfanilamide in war wounds. A first dose of 1.5 gm. given in solution for rapid absorption was advised; succeeding doses of 0.5 gm., starting two hours after the first dose, should be given every four hours as intact tablets to prolong their effect. Administration of the first dose as soon as possible after wounding is essential in order to combat the gas-gangrene organisms which are implanted at the time of injury and which develop rapidly. Prophylaxis must be continued for at least four days because many of the hemolytic streptococcal infections are caused later in the hospital. The danger of delay is stressed and it is pointed out that if several hours have elapsed before treatment begins, the first few doses should be increased. The use of proseptasine or of coated tablets to secure more prolonged retention of the drug did not seem to offer any advantages. WALTER H. NADLER, M.D.

# PHYSICOCHEMICAL METHODS IN SURGERY

## ROENTGENOLOGY

**Maier, H. C.: Roentgen Aspects of the Upper Retro-Esophageal Pulmonary Borders.** *Am. J. Roentgenol.*, 1940, 43: 168.

In the upper portion of the thorax, posterior to the esophagus, the right and left pleural spaces closely approach one another under normal conditions. An appreciation of this anatomical fact is of importance in the interpretation of roentgenograms because the pulmonary borders in this region are sometimes outlined roentgenographically. Various physiological and pathological conditions may displace the medial pleural margins and cause difficulty in the identification of the roentgen shadows. Anatomical studies on cadavers to show the limitations of the pleura in this region are discussed at some length and previous roentgenographic observations are also given consideration.

Although ordinary chest roentgenograms may not reveal the medial pulmonary borders in the upper posterior portion of the thorax, dense ones produced with the aid of the Potter-Bucky diaphragm sometimes show them. In such cases they present as curved margins of aerated lung close to the midline of the spine superimposed upon the air-outlined tracheal shadow. In lateral projections pulmonary tissue in the retro-esophageal space is seen to best advantage. It is evident especially when kyphosis is present.

Pathological conditions may produce displacements of these medial borders. Scar-tissue contracture may cause traction to either side, which may be accompanied by a tracheal and esophageal shift. Inequalities in the intrapleural pressures of the opposing hemi-thoraces may also displace the structures, and such herniation may be incorrectly interpreted as representing a pulmonary cavity or emphysematous bulla of the other lung. Sometimes posterior pulmonary borders are misinterpreted for medial margins of the lung anteriorly. Except under most unusual circumstances, the pleural borders do not approach the midline anteriorly above the superior margin of the manubrium.

ADOLPH HARTUNG, M.D.

**Doub, H. P.: The Roentgenological Aspects of Bronchomycosis.** *Radiology*, 1940, 34: 267.

The roentgen manifestations of the bronchomycoses are so protean as to defy exact classification in most instances. The classification of the bronchomycoses given by Castellani is quoted.

The pulmonary lesions of blastomycosis are less common than the lesions involving other viscera and the skin. The clinical picture often simulates that of tuberculous infection; to make a positive diagnosis the presence of blastomycetes must be demonstrated in the lesions themselves. The pulmonary roentgenogram may reveal considerable increase in the hilar areas and in the bronchovascular markings, with an unusual studding following these markings. The characteristic studding follows one or more of the main trunks, but does not quite reach the periphery. There is usually an area of lung density around the periphery. Some of the findings may suggest miliary tuberculosis, except that there is more fibrosis. One illustrative case is reported, in which there was extensive miliary parenchymal infiltration throughout both the lungs with areas of coalescence in the bases.

About 15 per cent of the cases of actinomycosis observed clinically involve the thorax. Pulmonary infection is often secondary to infection in other parts of the body. The roentgen findings are not characteristic; areas of consolidation are present, and in some instances there are localized nodules. If there is pleural involvement, fluid may be present in the pleural cavity. Abscess cavities may be found in the lung. The diagnosis is made by the finding of sulfur granules in the sputum. One case is reported as follows:

A boy of seventeen had abdominal actinomycosis, and there were several draining sinuses over the abdomen. Pulmonary roentgenograms revealed a large, smooth, rounded shadow of increased density in the base of the right lung just above the diaphragm; this mass diminished but did not entirely disappear after roentgen therapy.

Monilia may be the cause of primary bronchopulmonary disease, but it may also be present as a secondary invader in cases of primary bacterial infection. Variable changes are found in the lungs. The hilar areas are usually enlarged, and infiltration of a patchy type may extend from these areas throughout the lungs, being usually less marked in the apices. An extensive network of fibrotic infiltration, and studding along the bronchovascular markings, often extend throughout the lungs. In the patient here reported, there was, in addition to the bilateral hilar enlargement and diffuse pulmonary fibrosis, pleural reaction along the axillæ.

Aspergillus is not common in this country as a cause of primary pulmonary disease, but it has occasionally been noted as a secondary invader.

Penicillium and mucor are other filamentous fungi which are of clinical importance, but they are usually secondary invaders. One case in which penicillium infection was probably not the primary cause of death is reported.

Some of the literature on coccidioidal granuloma and streptothricosis is reviewed. It is important when a patient is encountered who has symptoms suggestive of, but somewhat atypical for, tuberculosis, and who presents atypical roentgen findings to make repeated microscopic examinations and to culture the sputum. HAROLD C. OCHSNER, M.D.

**Hartung, A.: Pulmonary Involvement in the Lymphoblastomas, With Special Reference to Roentgen Aspects.** *Radiology*, 1940, 34: 311.

Although some writers have included more separate entities under the term "lymphoblastoma," the author has included for the purposes of this paper only Hodgkin's disease, lymphosarcoma, and chronic lymphatic leucemia. Thirty-five cases are reviewed, including 24 of Hodgkin's disease, 6 of lymphosarcoma, and 5 of chronic lymphatic leucemia.

On the basis of this study, it is concluded that pulmonary involvement is so common, and the roentgen findings are so characteristic, that routine chest examination is indicated in patients who have lesions apparently limited to the superficial nodes. Tumorous masses in the mediastinum, with or without enlarged hilar nodes, and pulmonary infiltrations usually in close proximity to them are strong probable evidence that the condition is of this nature, especially if the changes are bilateral.

HAROLD C. OCHSNER, M.D.

**Levene, G., Lowman, R. M., and Wissing, E. G.: Roentgen Diagnosis of the Strawberry Gall Bladder.** *Radiology*, 1940, 34: 391.

The strawberry gall bladder (cholesterosis or lipoidosis of the gall bladder) is one of the earliest forms of gall-bladder disease. On roentgenographic examination, these gall bladders show good visibility and complete emptying of the dye, as do normal gall bladders. As a consequence, many strawberry gall bladders are diagnosed "normal" or "negative." The authors analyzed a series of 30 proved cases of strawberry gall bladder, and determined in what way they differed on roentgenological examination from normal gall bladders.

The diagnosis of strawberry gall bladder depends on the following criteria: good visibility, active contractions, good compressibility, local and reflex tenderness, and rapid emptying. In discussing these criteria, it is pointed out that good concentration of dye was invariably present; if poor concentration was present the cases were classified as chronic cholecystitis. Likewise, all gall bladders in this proved series exhibited active contractions, as contrasted with the poor or absent contractions seen in chronic cholecystitis. These contractions were best seen after the administration of a motor meal consisting of 4 egg yolks, and 8 oz. of 40 per cent cream flavored with ginger ale. Roentgenoscopic observations were made routinely, this procedure enabling the observer to determine the elasticity and compressibility of the gall bladder by "stripping" it between the two index fingers. Motility after a motor meal as well as local tenderness was noted on roentgenoscopic examination also. Local tenderness was detected in 90 per cent of the cases in this series. Reflex tenderness in the right costomuscular angle was found in 92 per cent of cases. This local and reflex tenderness is of considerable diagnostic import.

The strawberry gall bladder empties much more rapidly after a motor meal than a normal or chronically diseased gall bladder. It was found that, on the average, the normal gall bladder empties in four hours, the strawberry gall bladder empties in one hour and twenty minutes, and a chronically diseased gall bladder requires five or more hours to empty. This rapid emptying of the strawberry gall bladder is of great diagnostic significance.

The authors believe that many cases of early gall-bladder disease are erroneously diagnosed as "negative," and urge that close attention be focused upon this problem.

LUTHER H. WOLFF, M.D.

**Horwitz, T., and Smith, R. M.: An Anatomical, Pathological, and Roentgenological Study of the Intervertebral Joints of the Lumbar Spine and of the Sacro-Iliac Joints.** *Am. J. Roentgenol.*, 1940, 43: 173.

The value of the oblique projection of the lumbar spine as indicated by studies of various authors is given consideration at some length. The authors made studies of specially prepared specimens of 25 human adult male lumbar spines and pelves and arrived at the following conclusions:

1. Facets and apophyseal (intervertebral) joints of the lumbar spine the axes of which are other than 45 degrees from the sagittal plane may falsely appear to be the site of pathological processes in the routine 45 degree oblique views. In 13 of the 25 specimens, although the apophyseal joints were grossly uninvolved, the 45 degree oblique roentgenogram strongly suggested pathological changes; in all of these specimens the angle of the joint line, measured from the sagittal plane, exceeded or was less than 45 degrees.

2. Accessory ossicles (epiphyses) at the tips of the articular facets are frequently not visualized on the roentgenogram, and one may infer that fractures in this region might also remain undiagnosed.

3. Degenerative changes in the intervertebral discs are noted on the roentgenogram only after they are advanced and associated with narrowing of the intervertebral space and marginal bony proliferation.

Nuclear herniations into the vertebral body are visualized only when they are surrounded by a zone of osseous sclerosis. Herniations of the intervertebral disc into the vertebral body (Schmorl's cartilage nodes), measuring from 4 to 8 mm. in diameter, were present grossly and evident roentgenographically in 3 instances; they were not visualized on the roentgenogram, although present in the gross specimen in 3 other instances.

4. Subluxations of the articular facets, as described by Hadley, occur most frequently with narrowing of the posterior part of the intervertebral disc. Apparent subluxations in the presence of intervertebral discs of normal height are due to bony proliferation of the articular margins of the facets.

5. The diagnosis of degenerative changes, especially of ankylosis of the sacro-iliac joint, by means of the roentgenogram is frequently not corroborated by actual dissection. The 45 degree oblique projection

penetrated directly through the upper part of the joint space in only 6 of 28 normal sacro-iliac joints.

6. The oblique view of the lumbar spine is valuable in visualizing marginal proliferation of the vertebral bodies, which is usually most advanced anterolaterally; and it is an additional method in diagnosing impingement of the fifth lumbar transverse process against the sacrum or ilium.

Studies of the articular facets and apophyseal joint spaces in other projections were also made and findings which indicate the most favorable conditions for obtaining the desired information are presented. Detailed data of 80 lumbar spines and pelves examined are tabulated and numerous illustrations of dry specimens are included to demonstrate anatomical variations. Anomalous and pathological changes found are also described. Investigation of 100 adult lumbar spines in relation to accessory articular processes revealed accessory facets, unilateral or bilateral, single or multiple, in 14.

Experimental studies of vertebral bodies were also made and are described with a view toward obtaining information which might be of value in the roentgen diagnosis of intervertebral-disc herniations into the vertebral bodies. The following factors were found to determine the visibility of a bony defect in the roentgenogram:

1. State of calcification or trabecular condensation of the surrounding bone.
2. Content of the defect.
3. Relative amounts of cortical and spongy bone overlying the defect.
4. Diameter of the transradiated bone which is superimposed over the defect.
5. Distance of the defect from the tube and from the film.
6. Direction of the longest axis of the defect in relation to the central roentgen-ray beam.

Anatomical, pathological, and roentgenological observations on the sacro-iliac joint were also made and are described in detail. In 100 pelves studied, degenerative changes, consisting of articular cartilage and marginal bony proliferation, were seen in 37 specimens, and ankylosis of the sacro-iliac joint was present in 21 specimens. The variations and irregularities in the contour of the articular surface of the sacro-iliac joint, and the deviations in the plane of the joint surface at various levels of the joint in the same specimen and in different specimens, indicate that no one roentgenographic projection may be depended upon for its accurate visualization.

ADOLPH HARTUNG, M.D.

**Maxfield, J. R., Jr., and Martin, C. L.: The Evaluation of Roentgen Therapy in Sinus Disease.** *Radiology*, 1940, 34: 300.

No method of treatment of diseases of the accessory nasal sinuses has been entirely satisfactory, but conservative treatment should be tried first, inasmuch as poor medical results can be supplemented by surgical procedures, but poor surgical results cannot easily be corrected by medical treatment. The greatest benefit to be obtained from roentgen irradiation of the sinuses is in the hyperplastic type of sinusitis in which roentgenographs show thickened membranes and the patients have a thin watery discharge from the sinuses, frequent colds, or chronic cough. The shorter the duration of symptoms, the greater the chance of good results, and the greater the possibility of permanent cure.

The authors liken the response of the thickened hyperplastic sinus membranes to the response of keloids to roentgen therapy. The longer the duration of either, the less the likelihood of relief. They advise the use of roentgen therapy following radical operations on the antra, for they believe that this will prevent the return of the hyperplastic tissue, just as it does after the removal of keloids. Roentgen therapy should be used only after the use of conservative measures by a competent otolaryngologist, and should be used in co-operation with, rather than in competition with, the work of this specialist. The patient should be informed of the uncertainty of good results. Irradiation therapy is definitely contraindicated when there is not good drainage through the natural ostium or through "windows" in the sinuses, or in patients who have a tumor mass in the sinuses, inasmuch as the latter might be malignant.

After treatment the patient usually experiences a feeling of fullness in the face, and an increased discharge for from twenty-four to seventy-two hours. After this period, the discharge is diminished in amount, and thicker. If pain is present, it is usually relieved in seventy-two hours. Those patients who experience relief in from twenty-four to forty-eight hours after treatment usually get the best results. The maximum response is usually reached in from three to four weeks following therapy. Of 16 acute, uncomplicated cases, 7 were cured and 8 were improved. Of 9 acute, complicated cases, 5 were unchanged and only 1 was cured. Of 18 chronic uncomplicated cases, 9 were unchanged, 6 were improved, and only 2 were cured. Of 14 chronic complicated cases, 12 were unchanged after irradiation. The authors conclude that although roentgen therapy does give relief in a certain percentage of cases, it is not a panacea for all sinus diseases.

HAROLD C. OCHSNER, M.D.

**Peck, W. S., and McGreer, J. T., with Kretzschmar, N. R., and Brown, W. E.: Castration of the Female by Irradiation: The Results in 334 Patients.** *Radiology*, 1940, 34: 176.

The authors have made studies of the records of 334 patients who were treated for benign lesions with roentgen rays or radium, with the following objectives:

1. Determination of the efficiency of castration by radiation methods.
2. Establishment of the required ovarian dose for permanent castration.
3. Development of a treatment technique to deliver a known and constant dose of radiation to the ovaries of any patient.

4. Determination, if possible, of the ovarian dose for temporary castration.

Details of the different techniques of irradiation used, methods on which calculations of dosages were based, and findings which served to answer the objectives sought, are discussed at considerable length.

The following conclusions were drawn:

1. A dose of about 625 roentgens delivered to the ovaries produced permanent castration in the whole group of 72 patients.

2. In 34 (94 per cent) of 36 patients, there was permanent castration with from 500 to 624 roentgens delivered to the ovaries.

3. In this series even comparatively small doses of radiation to the ovaries produced permanent castration in a majority of cases. It appears that temporary castration cannot be produced with any degree of dependability.

4. A formula has been developed for calculating the surface dose to multiple ports necessary to produce a planned ovarian dose when ports of various sizes and different depth-dose tables are used.

5. Techniques and dosage tables for patients with pelves of different sizes have been developed to deliver a uniform ovarian dose.

6. Cessation of benign uterine bleeding, whether due to abnormal ovarian stimulation or normal menstruation, can be accomplished satisfactorily by irradiation of the ovaries.

7. There is no indication that irradiation castration results in serious impairment of health. The menopausal symptoms are no more severe or frequent than those which follow surgical castration.

ADOLPH HARTUNG, M.D.

**Pohle, E. A.: The Treatment of Infected Hemangiomas.** *Am. J. Roentgenol.*, 1940, 43: 408.

Radiation therapy, especially with radium, constitutes the method of choice in the treatment of vascular nevi. Very satisfactory cosmetic results are obtained in approximately 75 per cent of the cases. Only the port-wine nevus is unsuitable for irradiation.

In studying the results in a series of 152 patients with hemangiomas observed during the last decade at the Wisconsin General Hospital, the author became interested in the problem of secondary infection of these lesions. In order to obtain further information on this subject he mailed questionnaires to 30 well known radiologists and dermatologists throughout the country asking the following questions: (1) how many cases of infected vascular nevi have you seen? (2) what is the approximate percentage of incidence in your own cases? (3) do you recommend radium therapy of infected vascular nevi? and (4) if the answer to question No. 3 is in the affirmative, do you vary the dose as compared with non-infected vascular nevi? Replies were received from 14 sources, 12 of which were used in the present survey. The respective answers are arranged in the form of a table and to this the author adds the brief case reports of his 4 cases, several photographs being used for illustration.

The conclusions are that the incidence of secondary infection in vascular nevi is low as it varies from 0 to 5 per cent; in the author's cases it was 2.6 per cent. Infection does not constitute a contraindication to radium therapy, and if radium is applied the doses must be smaller and given at greater intervals than is customary in the non-infected vascular nevi.

T. LEUCUTIA, M.D.

# MISCELLANEOUS

## CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

**Young, F. G.: The Pituitary Gland and Carbohydrate Metabolism.** *Endocrinology*, 1940, 26: 345.

While the relationship of the pituitary gland to carbohydrate metabolism remains obscure, certain observations of the action of extracts made from the anterior lobe of this gland are beginning to bring the subject into light.

By treatment with anterior-lobe extracts an insensitivity to the action of insulin has been cultivated in normal and hypophysectomized animals. This anti-insulin effect is attributed to a "glycotropic" substance which, since it is not also diabetogenic, cannot be identical with the diabetogenic principle of the anterior lobe of the pituitary gland. However, it may be one part of a diabetogenic complex in which a number of active principles are concerned. Although not yet isolated, this substance, on the basis of available evidence, differs from prolactin and from the thyrotropic, gonadotropic, ketogenic, and melanophore-expanding substances of the gland.

A second effect, ketogenesis, produced in animals treated with anterior-lobe extracts, may be due to a specific ketogenic factor, although it must still be shown that the ketogenic factor and the growth and diabetogenic principles are not the same, or that the ketosis which occurs is not due to a diminution in carbohydrate and protein catabolism caused by the extracts.

A diabetogenic action which has been demonstrated in anterior-lobe extracts by the establishment of a permanent diabetic condition in normal dogs is thought to be due to a principle which differs from prolactin and the thyrotropic, gonadotropic, "glycotropic" or melanophore-expanding substances of the gland. This diabetic condition does not undergo spontaneous remission. Although the animals are able to survive for long periods without insulin therapy, some of them may require more insulin to control glycosuria than depancreatized dogs, and if the hormone is suddenly withdrawn after the animal has received insulin therapy for a period, the animal may die in a state which resembles diabetic coma.

An increase in the size and number of the islets of Langerhans has been observed in the rat pancreas after injections of anterior-lobe extracts. Since this cannot be entirely explained as a compensatory reaction to the diabetogenic factor, the existence of a fourth, pancreotropic, action of the anterior lobe must be considered.

The author suggests that since diabetogenic preparations from the anterior lobe have been observed to possess growth-promoting activity, it is barely possible that the growth substance and the diabetogenic principle may be closely related if not identical. The diabetogenic action may become manifest in those cases in which the pancreas secretes insufficient insulin to induce nitrogen retention and promote carbohydrate oxidation, and the growth-promoting action may be exhibited in those animals that can elaborate an adequate amount of insulin.

EDWARD W. GIBBS, M.D.

**Soskin, S.: The Liver and Carbohydrate Metabolism.** *Endocrinology*, 1940, 26: 297.

The origin of blood sugar from non-carbohydrate precursors in the fed or fasting animal is not clearly understood. After careful analysis of the results obtained by studies of the D:N ratios in experimental animals, the author concludes that sugar is derived partly from protein but that this is not the only source. The dextrose component of the D:N ratio represents the net remainder after the extrahepatic utilization of sugar is subtracted from the hepatic blood-sugar formation. Once this is granted, it may be concluded that the breakdown of protein cannot supply sufficient sugar for both excretion and utilization, and therefore the liver must form sugar from fatty acids as well as from protein.

There is much evidence to indicate that carbohydrate utilization in the diabetic organism is not as markedly impaired as one might suppose. If the utilization of carbohydrate was not a factor in the D:N ratio of the whole diabetic animal, similar D:N ratios should be obtained by experiments with isolated livers, but this is not the case.

The respiratory quotient of the body as a whole, like the D:N ratio, is also not the index of a single process. The interpretation of the non-protein R.Q. of 0.7, which is characteristic of the fasting and the diabetic states, involves the assumption that the only vital processes which consume oxygen and give rise to carbon dioxide, except protein catabolism, are those associated with the oxidation of fat. However, there is adequate proof that other processes which require oxygen or yield carbon dioxide occur under these same conditions. Since the R.Q. appears to be of a composite nature, it is difficult to justify the accepted interpretation of a 0.7 value in view of the evidence which indicates that carbohydrate utilization proceeds under a variety of conditions in which this R.Q. is obtained.

The diabetic R.Q. can be interpreted best as a result of at least two factors: a low component resulting from the new formation of sugar from fatty acid and protein, and a high component due to the oxidation of that carbohydrate. Furthermore, since this gluconeogenesis occurs in the liver, the low R.Q. values obtained from determinations performed on isolated livers confirm this interpretation.

Ketosis in diabetes and other conditions has been attributed to either (1) products of incomplete fat oxidation which accumulate because of a lack of

simultaneously oxidizing carbohydrate, or (2) intermediate metabolites which appear during the conversion of fatty acid to sugar and accumulate in excessive amounts whenever the rate of gluconeogenesis from fat becomes abnormal. On the basis of existing evidence the author believes the second concept to be correct.

The ability of the body to rapidly adjust the blood-sugar level, which is represented by the normal curve of a dextrose tolerance test, has been explained in terms of increased sugar utilization and storage due to increased insulin secretion. The diabetic type of curve has been attributed to a lack of pancreatic response to the administered sugar and a consequent deficiency in sugar utilization and storage. However, from studies of depancreatized and hepatectomized dogs it appears that the liver and not the pancreas is the essential organ to the metabolic reactions which determine the normal dextrose tolerance curve. In the presence of adequate insulin the normal liver, after the administration of dextrose, decreases the output of blood sugar which it has been supplying from its own resources.

The coincident decrease in gluconeogenesis which accompanies the diminished output of sugar by the liver removes a low component of the composite R.Q. and thus explains part of the rise in the R.Q. which follows sugar administration. The stimulus which elicits the hepatic inhibitory response is the blood sugar itself, and the threshold of stimulation of the hepatic mechanism in a particular animal depends upon the endocrine balance of that animal and coincides with the level of blood sugar which it habitually maintains. EDWARD W. GIBBS, M.D.

**Cori, C. F.: Glycogen Breakdown and Synthesis in Animal Tissues.** *Endocrinology*, 1940, 26: 285.

Until recently little was known regarding the enzymatic processes concerned with the breakdown and synthesis of glycogen in liver and muscle. The author presents a brief review of the recent advances which have been made in the study of this problem.

An enzyme, phosphorylase, which initiates the breakdown of glycogen has been obtained from extracts of liver and other organs. This enzyme requires for its activity the presence of a coenzyme, adenylic acid, and acts in an anaerobic environment. It is thought to be a catalytic agent for the reaction between glycogen and phosphoric acid which results in the formation of glucose-1-phosphate.

This hexose phosphate in turn is acted upon by a second enzyme, phosphoglucomutase, also obtained from tissue extracts, which catalyzes the migration of the phosphate group from carbon atom No. 1 to carbon atom No. 6 forming glucose-6-phosphate.

A third enzyme obtained in tissue extracts, isomerase, is a catalyst for the conversion of glucose-6-phosphate into fructose-6-phosphate. When this reaction reaches a state of equilibrium, about 80 per cent of the substance is present as the glucose ester and 20 per cent as the fructose ester. The compound resulting is identical with equilibrium ester, a normal constituent of resting muscle and the end-product of glycogen breakdown in dialyzed extracts of muscle, heart, and brain.

Because certain differences exist in the decomposition of the glycogen in liver extracts and that in extracts of muscle, it is necessary to consider these two processes separately. In liver extracts glucose-1-phosphate and glucose-6-phosphate are reduced to glucose and inorganic phosphate. Liver, in contrast to muscle, contains a phosphatase which acts on the equilibrium ester to complete the process of blood-sugar formation.

In muscle, hexosemonophosphate is formed by esterification of glycogen with inorganic phosphate. In intact muscle the equilibrium ester under aerobic conditions is partly oxidized and partly converted to glycogen, and under anaerobic conditions is transformed to lactic acid.

In glycogen synthesis the first step, which occurs only under aerobic conditions, is a phosphorylation of glucose and fructose which results in the formation of hexose phosphate. However, the first products of this reaction have not yet been isolated. The completion of the process, namely, the conversion of glucose-6-phosphate to glycogen, although not yet obtained in tissue extracts, has been demonstrated in intact muscle.

The possible influence of epinephrine and insulin on these enzyme reactions is suggested, and it is hoped that additional investigations of a similar nature may eventually lead to an explanation of the mechanism of action of these and other hormones. EDWARD W. GIBBS, M.D.

**Broster, L. R.: Differential Diagnosis of Cushing's Syndrome (Basophilism) of Pituitary or Adrenal Origin.** *Brit. M. J.*, 1940, 1: 425.

In an attempt to point out the differences between the pituitary basophilism of Cushing and the adrenocortical syndrome, Broster emphasizes the point that the entire matter of the pathogenesis and primary locus of altered physiology is still an open question.

The syndrome of Cushing is characterized by two prominent features: changes in the sexual sphere and disturbances of the metabolism. The typical patient is a young woman who developes hirsuties of the male type, experiences menstrual irregularity or cessation, and becomes permanently fat in an abnormal distribution. In the male there is a similar abnormal adiposity, a loss of libido, and a decrease in the size of the genitalia. Secondary changes, showing a great variability, may take the form of low sugar tolerance, hypertension, erythrocytemia, cholesterolemia, and the appearance in the skin of striæ distensiæ.

The onset of the adrenocortical syndrome, on the other hand, is less likely to be accompanied by a gain in weight, though a transitory or moderate gain in weight is not unusual. The secondary metabolic changes do not appear; in the female, muscle will develop and secondary male sexual characteristics, typical of true virilism, will become prominent.

However, the onset and early phase of the two diseases may be very similar.

The author states that in the Cushing syndrome a typical basophilic hypophyseal lesion is present, and in Cushing's own series some of the patients showed adrenal hyperplasia as well. In "basophilism" of the adrenal type, the pituitary gland contains no basophilic adenoma, the adrenals are typically hyperplastic, and the tumor cells, in those cases in which a frank adrenal tumor is present, give a positive ponceau-fuchsin staining reaction. Other authors, as well as Broster, have found pregnanetriol and, among other ketosteroids, iso-androsterone in the urine of patients suffering from adrenal virilism. Such substances are not found in the urine of normal persons or of patients harboring a basophilic adenoma of the pituitary gland. These abnormal androgens have been greatly reduced by the removal of one hyperplastic adrenal gland, and frequently alleviation of certain of the symptoms follows.

Two illuminating case reports are given, one concerning a young male with pituitary basophilism, and the other a young woman with hyperplasia of the adrenal glands. JOHN MARTIN, M.D.

**Hamblen, E. C., Powell, N. B., Cuyler, W. K., and Pattee, C. J.: Oral Use of Pregneninonol in Functional Menometrorrhagia.** *Endocrinology*, 1940, 26: 201.

These authors report observations made on 7 young women with functional menometrorrhagia who were treated with pregneninonol, a derivative of estradiol in combination with estriol glucuronide and estradiol. After the menometrorrhagia of these patients had been controlled immediately by either curettage or by the injection of estrogens and progestrone, oral therapy was begun directly. Estradiol was given orally in doses of 2,400 oral units (2 mgm.) daily for fourteen days. Beginning on the fifteenth day sodium estriol glucuronide or estriol glucuronide was given in daily doses of from 1,800 to 3,900 oral units simultaneously with pregneninonol in daily doses of from 40 to 160 mgm. The latter combination was given for from ten to fourteen days and was discontinued when bleeding began. Observations during 14 cycles were reported as follows:

The clinical tolerance to pregneninonol in doses as large as 160 mgm. daily for fourteen days was good; bleeding of cyclic character and of normal amount occurred during this treatment. Endometrial biopsies taken at the onset of each menstrual period showed some degree of progestational response with this treatment, i.e., a mixed endometrium was observed in approximately 14 per cent of the endometria before therapy and in approximately 54 per cent during treatment. This therapy produced no significant alterations in the urinary titers of sodium pregnandiol glucuronide and of androgens of the patients investigated. The number of observations are too few and the period of observation too short to draw any definite conclusions.

RULON W. RAWSON, M.D.

**Liuzzo, G.: Parathyroidectomy in Scleroderma** (La paratiroidectomia nella sclerodermia). *Policlin.*, Rome, 1940, 47: sez. prat. 41.

Liuzzo describes 2 cases of progressive scleroderma in which parathyroidectomy was performed bilaterally in the first patient and unilaterally in the second, the immediate results being good but unfortunately only temporary. In the first case, the disorder presented the typical and not infrequent association with Raynaud's disease of the sclero-atrophic variety. The changes in the skin of the face appeared during a second stage when the fingers had already undergone severe alterations of the skin and of the nails with mutilation of the last phalanges over the course of many years. In numerous determinations, the calcemic values had varied within wide limits, but had always been above the level which is considered as physiological. Study of the sympathetic nervous system had revealed a slight increase in the sympathetic excitability. In the second case also, the calcemic values showed wide variations, but always in a hypercalcemic sense; on the other hand, the sympathetic nervous system was excitable especially in its parasympathetic section.

Parathyroidectomy was biochemically justified and offered the possibility of general and local amelioration because the cutaneous dystrophy, although typical, had not yet reached a stage that was too advanced and therefore irreversible. The resected parathyroids were found to be histologically normal. The immediate improvement of the cutaneous condition was more subjective than objective: there was a feeling of increased elasticity and softness of the skin, and of easier movements in the parts corresponding to the sites of the most marked changes; the skin of the hands could be lifted in folds to some degree. The calcemic values were not changed in the first case, but a decrease of about 20 mgm. per thousand without, however, reaching normal values was observed in the second case. The amelioration, which was very transitory in the first patient, has persisted for five months in the second, but is not fully confirmed by objective examination; further observation is needed to evaluate the intervals of relative well being.

It is difficult to offer a satisfactory explanation of the mechanism by which a decided feeling of improvement in the cutaneous condition occurs soon after the operation. This improvement, however, is not proportionately confirmed by objective findings. The theory that the amelioration is causally related to changes in the calcium metabolism seems to be denied by the present cases. Resection of one or more parathyroids in scleroderma has been performed in a sufficient number of cases to allow some theoretical and practical conclusions. In all cases but 1, the parathyroids were histologically normal. The intervention has not fulfilled the hopes founded on it. Besides, the increase in the calcemic rate, which led the first investigators to suspect a genetic relationship between a functional change in the parathyroids and scleroderma, is not the rule. Various

considerations suggest that there is not enough justification to consider human scleroderma as a form of chronic hyperparathyroidism with cutaneous localization. Certainly, the results of parathyroidectomy contradict any assertions of relationship between parathyroid dysfunction and scleroderma. The temporary improvement of the skin after parathyroidectomy is probably due to changes in the peripheral circulation determined by the sympathetic nervous system. It is possible that a functional disturbance of the parathyroids may in some manner be connected with the pathogenesis of scleroderma in its various manifestations and complications, but it would be irrational to exaggerate its rôle by resorting to surgical interventions of doubtful value. RICHARD KEMEL, M.D.

**Galloway, J. D. B., Broders, A. C., and Ghormley, R. K.: Xanthoma of the Tendon Sheaths and Synovial Membranes; a Clinical and Pathological Study.** *Arch. Surg.*, 1940, 40: 485.

Since 1919, 70 patients have presented themselves at the Mayo Clinic with one or more xanthomas of the extremities involving the tendon sheaths or synovial membranes. In this group 50, or 71 per cent, were women; 20, or 29 per cent, were men. The average age for the women was forty-five years, and for the men forty-three years.

The weight of each patient was determined to see if this group of patients were of an obese nature. It was found that in 37, or 53 per cent, there was a record of overweight, with an average of about 24 lb. overweight per patient.

There was a specific history of trauma in 31, or 44 per cent of the patients; 14, or 20 per cent, revealed the presence of arthritis in the involved extremity; and 6 patients had a history of both infection and trauma, which makes a total of 39, or 56 per cent, that had either an infectious or a traumatic background.

In 62 patients there was a record of the duration of the tumor, revealing an average duration of six years and one month.

In the 70 patients observed, there were 88 tumors. Sixty-five patients had 82 tumors of the tendon sheaths and 5 patients had 6 tumors of the synovial membranes.

The tumors of the synovial membrane were found in the knee, and only 1 was a real diffuse xanthoma.

The history elicited was usually the same, with patients complaining of a slow-growing, painless mass, very seldom causing any disability, except when the size was sufficient to produce mechanical block of the motion of a joint. Some of the tumors were preceded by injury, but often no history of a definite injury could be determined.

On physical examination, the usual picture was that of a subcutaneous, firm mass, of varying size and shape, not tender on pressure and located in the vicinity of the tendon sheaths, or on them. The overlying skin was unattached, but evidence of attachment to deeper structures was present. Even if it was quite evident that the mass was fastened to the sheath, the motion of the tendon in the sheath was not hampered.

The results of the routine laboratory tests were all essentially negative with regard to this condition.

Sixty-nine of the 70 patients were treated surgically at the Mayo Clinic. Sixty-seven patients were treated by local excision alone and 8 had roentgen treatment in addition to local excision. Roentgen treatment was given only in those cases in which it was believed that all of the tumor had not been or could not be completely removed.

Most of the tumors were quite easily shelled out intact and without much damage to the tissues.

Grossly these tumors appeared as round or ovoid, practically always lobulated, well encapsulated, solid masses, of moderately firm to quite firm consistency, and of a color varying from grayish-yellow to yellowish-brown and reddish-brown.

Microscopically, their appearance varied. There were, however, certain definite characteristics which were nearly always found: for example, the foam cells, foreign-body giant cells, pigment, and fat.

The type-cells of the stroma were the same in all instances. They were polyhedral, oval, or round, containing one nucleus that was usually quite large and either round or oval. Each nucleus stained lightly and contained one and sometimes two darkly stained nucleoli. The cytoplasm of these cells took the eosin stain faintly and was of a rather homogenous and slightly granular nature. These cells looked not unlike endothelial cells and were arranged usually in solid masses, separated only by the interlacing strands of fibrous tissue. Some spindle cells were present in small numbers, and very few polymorphonuclear leucocytes were observed in any one section.

Foam cells were found in all but 8 tumors. These cells were of varying size and shape; their cytoplasm revealed a granular, foamy appearance; and their nuclei were smaller than those of the type-cell, having a shrunken, pyknotic appearance.

Giant-cells of the foreign-body type were found in all but one patient. They varied in size and shape, but a rectangular cell seemed to predominate.

There was evidence of a good blood supply in all the tumors.

The authors conclude that xanthoma is a slowly growing, painless type of tumor, taking usually years to develop, five years and one month on the average in those cases reviewed in the literature, five and a half years in their own cases. It causes no disability except when it reaches a size large enough to interfere mechanically with adequate motion of the joints or proper function of the extremities. It is of varying size and shape but in most cases is a firm, round or oval lesion, averaging in size from 2.5 to 3 by 2 cm. It is slightly smaller on the hands and fingers than on the feet and ankles. It occurs on the upper extremity from two to three times as often as on the lower, involving the finger most frequently. It is most common on the index and middle fingers, as shown by both series of cases.

The authors say that given a man or woman about forty years of age, with a firm, oval or round, subcutaneous mass from 2 to 3 by 2 cm. in size, located on or associated with a tendon sheath, preferably the flexor of the fingers, a mass that has been painlessly, slowly increasing in size; and, moreover, if the patient presents a history of previous trauma and his blood chemistry reveals an absolute increase in its lipoids or an alteration of the ratio of cholesterol to cholesterol esters, you will have, in all likelihood, a xanthoma of the tendon sheath.

This tumor must be differentiated from chondroma, which is harder; lipoma, which is softer; carcinoma, which usually affects the skin; osteoma, which is harder and connected with the bone, and from ganglion, which is usually on the extensor surface, near a joint, and softer in consistency. Tumors of the muscle must be thought of, and tendovaginitis and tuberculous dactylitis are possibilities which must be considered.

Since these tumors have been definitely proved to be benign without evidence of metastasis, the authors consider conservative surgical treatment to be the one of choice. Usually only a local excision is necessary; if a recurrence takes place (it does if the tumor has not been completely excised) a second excision should be performed. However, a limb should never be sacrificed for what appears to be a sarcoma at first glance. The actual value of roentgen therapy in the treatment of these tumors is still questionable, and in most cases very little, if any, response has been observed; however, this method will probably continue to be used as an adjunct to surgical removal and perhaps in the future might prove to be of benefit in those cases in which complete removal of the tumor is not possible.

**Campbell, J. A.: The Influence of Low Oxygen Pressure upon the Incidence of Primary Lung Tumors in Mice.** *Brit. M. J.*, 1940, 1: 336.

The author reports a series of low-oxygen-pressure experiments which seem to be the first of their kind to throw any light on the influence of low oxygen pressure in the atmosphere upon the incidence of primary lung tumors. These experiments were begun in London on December 9, 1936, and continued until September 2, 1939, when, unfortunately, at the outbreak of the war, it became necessary to discontinue them because of the danger of fire from the oxygen. During this period, however, some useful information had been obtained, which is recorded in the present paper.

Several observers have suggested, with respect to cancer in general, that tumors originate in cells suffering from oxygen deficiency, while others have found that general oxygen deficiency inhibits the growth of tumors but does not destroy the cancer cells completely. It is quite possible, however, that the origin of the cancer cell may be controlled by factors differing from those controlling the rate of growth of the resulting tumor. So far, most of the evidence tends to show that tumor growth is more rapid in a host with favorable conditions as to general nutrition.

The author states that if low oxygen pressure plays a part in the production of so-called spontaneous tumors, then exposure of animals for long periods to an atmosphere with an abnormally low oxygen pressure should increase the incidence of the tumors. In the course of an investigation of the powers of acclimatization of mice to low oxygen pressure, an opportunity presented itself to study the incidence of primary lung tumors under subnormal oxygen pressure. It is a frequent observation that lung tumors in mice appear to originate in a collapsed or thickened area. It is presumable that the cells in the center of such an area might suffer from some degree of anoxia. This will be increased in degree if the animal breathes oxygen at a lowered pressure. Age has an effect on these lung tumors, which are rare in mice less than ten months old. This is similar to the findings pertaining to human lung cancer, in which the mean age at death is fifty-five years. The author states that obviously a man who dies of cancer of the lung is susceptible to it, and that therefore it serves no good purpose to use non-susceptible animals for experiments. Accordingly, in experiments with mice, attention should be directed particularly to the incidence of lung tumors in those which are older than ten months.

The author fully describes the methods used in conducting his low-oxygen-pressure experiments with mice placed in a respiration chamber and subjected to low oxygen pressure. The experiments were fully controlled by a number of mice placed in a similar respiration chamber and subjected to the same conditions except that they were exposed to normal oxygen pressure, namely 20.9 per cent of an atmosphere.

A record of the duration and percentages of oxygen pressure in the chamber with subnormal oxygen pressure brings out some interesting data. Mating of the mice was allowed, and it was found, upon lowering the oxygen pressure to 14 per cent of an atmosphere, that the females became pregnant but refused to rear their young. Therefore, the oxygen pressure was raised to 15 per cent and kept at this level for three hundred and fourteen days. After some time at this level the mice reared their young and a lowering of the oxygen pressure to 14 per cent was again instituted. After thirty-nine days at this level the oxygen pressure was lowered to 13 per cent, at which level it was maintained for three hundred and seventy-nine days, or until the experiments were stopped.

The results of these experiments, as far as they go, indicate that anoxia increases the incidence of primary lung tumors in mice older than ten months, and may therefore be a factor in the origination of tumor cells. The results also prove that it is possible to acclimatize mice to 13 per cent of oxygen, equivalent to an altitude of about 15,000 feet, so that they breed and rear young which grow at a normal rate under this low oxygen pressure.

MATHIAS J. SEIFERT, M.D.

**Bade, W.: Metastatic Carcinoma of the Skin Following Carcinoma of the Internal Organs** (Das metastatische Carcinom der Haut im Anschluss an Carcinom innerer Organe). *Arch. f. Dermat. u. Syph.*, 1939, 179: 257.

To his own observation of carcinoma of the internal organs which metastasized to the skin, the author adds 58 cases gathered from the literature. Such a sequence was published the last time in 1913.

In the author's case a woman began bleeding twenty years after the menopause. She sought medical advice on account of the bleeding of knotty swellings in the skin of her abdomen. These tumefactions proved to be metastases of an adenocarcinoma. The patient died while the clinical examinations of her condition were being conducted.

Skin metastases appear clinically either as knotty or flattened sclerodermic-like infiltrations, and are most frequently multiple; they are partly cutaneous and partly subcutaneous. The skin is livid brown to dark red and ulcerates readily. The cancerous cells of the metastases retain the characteristics of the primary tumor. The diagnosis of a skin metastasis not infrequently leads to the diagnosis of the primary cancer, even though in some cases the site of the primary tumor could not be established clinically. In recent years cases of skin metastases following genital carcinomas seem to appear more frequently. Why skin metastases occur in some cases is not yet understood. The summary of these cases offers very interesting details.

(Hirsch-Hoffmann). Mathias J. Seifert, M.D.

**Peller, S.: Life Expectancy and Mortality from Skin and Lip Cancer.** *Am. J. M. Sc.*, 1940, 199: 449.

In order to estimate the life-shortening rôle of skin and lip cancer one can depend less on the causes than on the frequency of death and on the time elapsed since the onset of the illness. In this paper such an attempt has been made. The author studied 715 cases; all were included, whether treated or not.

The following conclusions are made:

At the onset of the disease, carriers of an epithelioma of the skin or lip are about as old as the average of all other cancer patients. At the time of death they are older. The influence upon the life expectation and mortality depends on the age at onset. Patients with skin and lip cancer less than sixty years old had in the author's material an increased mortality and a shortened life expectancy, as compared with the average population at the same age. Patients with onset of the epithelioma at ages above seventy years had a lower mortality and a higher life expectancy.

At the beginning of the "cancer age," at forty, the total group of future carriers of a surface cancer have most probably a future life surplus, compared with the total population of the same age. This indicates that the primary internal cancers developing in those who already have or have had surface cancer are not frequent enough to diminish the life expectancy in this group or to frustrate the value of therapy of the surface malignancies.

Joseph K. Narat, M.D.

**Peyton, W. T.: Danger in the Use of Local Infiltration Anesthesia in Operations upon Malignant Tumors.** *Ann. Surg.*, 1940, 111: 453.

There are certain clinical procedures which when improperly performed may tend to produce metastases, i.e., biopsy, palpation of tumor, and operation for removal of tumor. The clinical impression has been gained that local infiltration anesthesia may occasionally cause dissemination of malignancy. This impression came from the occasional case of carcinoma which developed an extensive local dissemination or metastases to regional nodes after operation under local infiltration anesthesia.

To check this impression, animal experiments were carried out by inoculating various tumors into mice and when the tumors had reached a proper size they were divided into control and experimental groups. The tumors in the control group were removed under general anesthesia at approximately the same interval after inoculation as the tumors in the experimental group, the latter also being removed under general anesthesia, but in addition 1 c.cm. of a 0.5 per cent solution of novocaine was injected about the tumor in the experimental animals.

The experiments would seem to indicate that the common surgical practice of using local infiltration anesthesia for biopsy or removal of malignant tumors is a dangerous procedure and should be discontinued. Joseph K. Narat, M.D.

**Dodd, H.: Drugs Used in Surgery to Raise the Blood Pressure, with Special Reference to Veritol.** *Lancet*, 1940, 238: 358.

Coramine, adrenaline, icoral, eserine, ephedrine, and cortin have been employed for elevation of the blood pressure during surgical procedures, but except for ephedrine their use was not suitable. Despite the need for repeated intravenous injection of ephedrine, it remained the chief remedy until something better was found.

Veritol ($\beta$-p-oxyphenyl isopropylmethylamine) has proved most satisfactory for raising the blood pressure. It may be given intravenously, intramuscularly, or by both methods. The dose for intramuscular injection is from 0.75 to 1.0 c.cm. The blood pressure begins to rise in from three to five minutes and reaches a maximum in twenty minutes. The fall from this level takes place during the succeeding twenty to forty minutes, when the dose may be repeated. In severe shock the dose may need to be 1.5 c.cm.

A dose of 0.25 c.cm. given intravenously will give a response within fifteen seconds. The effect is quick although the subsequent fall is quicker than following intramuscular injection, so a combined dose is employed: 0.25 c.cm. given intravenously and 0.75 c.cm. given intramuscularly.

Cardiazol and veritol have been given together in patients who are cold, whose nails are dusky, whose systolic pressure is near or at the diastolic level, and whose pulse is weak.

Hypertonic saline solution (30 per cent) has also been used effectively in raising blood pressure after the use of spinal anesthesia.

JOHN WILTSIE EPTON, M.D.

## GENERAL BACTERIAL, PROTOZOAN, AND PARASITIC INFECTIONS

**Carroll, G., Kappel, L., Jones, L., Gallagher, F. W., and DiRocco, F. W.: Sulfamethylthiazol: A Report of Its Clinical Use in Staphylococcus Septicemia with Apparent Success. Report of Animal Experiments.** *South. M. J.*, 1940, 33: 83.

The authors report for the first time the successful use of a sulfanilamide derivative, sulfamethylthiazol, for combating staphylococcus aureus infections and septicemia.

There have been a few reports in the literature of recovery from staphylococcus septicemia with the use of sulfapyridine. According to Perrin Long, who reported the first use of sulfanilamide against the streptococcus, the use of sulfapyridine is only mildly effective in staphylococcus bacteriemia. In the group which he reported 3 of 5 patients with this disease recovered.

Five cases are reported here, 1 of an elderly man with staphylococcus aureus infection of the kidney. Consecutive trials of mandelic acid, sulfanilamide, and sulfapyridine produced no change in his toxic state. At operation, a diffuse infection of the perirenal tissue was found; there was drainage of thick yellow pus. On the fourteenth postoperative day sulfamethylthiazol was given in doses varying from 6 to 14 gm. daily. After medication for twenty days with this drug, the urine became negative. Rapid defervescence of the disease occurred. According to the authors, at no time was a positive blood culture obtained.

In 2 cases, which were classed as mild pyelonephritis due to staphylococcus aureus, negative urine cultures were obtained after one week of use of this drug. These ambulatory cases showed no toxic symptoms of the drug.

One case of staphylococcus septicemia in a young woman who developed a breast abscess during the puerperium was first treated with sulfanilamide with no relief. After blood transfusions together with soluble sodium sulfamethylthiazol administered intravenously, the blood culture became negative and recovery occurred.

In the fifth case, that of a ten-day-old male infant, staphylococcus septicemia developed from an infected umbilicus. No effect was produced by neoprontosil or by sulfapyridine. The septic process involved the left knee joint, right shoulder joint, and right hip joint in succession. Sulfamethylthiazol was given, and septic symptoms promptly subsided within twenty-four hours. The infant recovered, but when last seen had a necrosis of the head of the right humerus.

The authors carried out experiments on mice. The animals were given intravenous injections of virulent staphylococcus aureus. The result was that about 70 per cent of the animals given sulfamethylthiazol or its sodium salt had a survival time of fifteen days, whereas in the non-medicated animals the average survival time was from three to four days.

In the discussion Carroll points out that very thorough animal and test-tube experimental work had been carried out in the research department of the Winthrop Chemical Company, and the workers had administered 4 gm. daily of the drug to themselves without deleterious effects.

JOHN E. KIRKPATRICK, M.D.

## DUCTLESS GLANDS

**Collip, J. B.: The Physiology of the Anterior Pituitary and a Note on the Medullotrophic Hormone.** *Am. J. Obst. & Gynec.*, 1940, 39: 187.

The number of true anterior-lobe hormones must be very small, which is in keeping with the anatomical nature of the "factory" which produces them. The author lists 15 physiological effects attributed to the pituitary gland. All of the physiological activities of the anterior lobe are represented by different groupings in two or three protein substances secreted by the gland. Growth of various organs may be largely independent of the pituitary growth hormone and the function of the latter would seem to be the regulation of the increase in the size of the body as a whole with a harmonious and proportional increase in the size of all the organs. Since no absolutely pure growth hormone either in the chemical or the physiological sense has been obtained, it is difficult to decide just what physiological effects are related to this substance and not to any other.

A clinical trial of the specific metabolic factor in a small group of obese women showed some rather unexpected results. It so happened that most of the subjects treated had some degree of menstrual irregularity, and in 4 of 8 cases treated the patients stated, without any leading question, that it was the first time in years that they had noted any regularity at all.

Probably the most important of the investigations relating to the physiology of the pituitary gland led to the finding of a medullotrophic principle in primary alcoholic extracts of prime gland tissue. This principle has also the remarkable quality of being active orally. It appears to be trophic to the so-called "dark cells" of the adrenal medulla. All of the evidence so far available seems to show that this orally active pituitary principle does not act upon the chromaffin system. Since potent preparations of the corticotrophic hormone satisfactory for administration by injection to the human subject can now be made, and since the medullotrophic substance can be administered safely by the oral route, the clinician will have two agents, each of which can

be biologically standardized, with which to influence at least two functions of the adrenal glands.

EDWARD L. CORNELL, M.D.

**Coggeshall, C., and Root, H. F.: Acromegaly and Diabetes Mellitus.** *Endocrinology*, 1940, 26: 1.

Twenty-nine cases of combined acromegaly and diabetes are reviewed. An average interval of nine and two-tenths years was found between the onset of acromegaly and that of diabetes. The existence of hereditary or familial diabetes in 6 of the 29 cases, or 21 per cent, suggested a predisposition to diabetes. Among relatives of 127 non-diabetic acromegalics, a history of diabetes could be obtained only in 2 per cent of the patients. In groups of patients with acromegaly, diabetes, a combination of both conditions, and Simmonds' disease, comparative studies of the weights of organs at autopsy showed splanchnomegaly only in the presence of acromegaly. The possibility of permanent damage to the islands of Langerhans as the result of a brief period of acute hyperpituitarism is admitted, although in 4 cases of fugitive acromegaly caused by mixed pituitary tumors, diabetes failed to develop. In 50 autopsies of diabetics variations in the size of the pancreas were not associated with variations in the weights of other internal organs, as was the case in acromegaly and Simmonds' disease.

Clinically, the diabetes in acromegalics showed no greater variations in severity, duration of life, or resistance to insulin, than were observed in a large group of ordinary diabetics. The usual complications of diabetes occurred. It was noted that in patients who had repeated insulin reactions, blood-sugar curves might suggest insulin "sensitivity." Some acromegalic diabetics developed coma; other individuals with polyphagia, but with no loss of weight or acidosis, had diabetes not unlike that produced in dogs by Young, by means of the injection of large amounts of crude anterior pituitary extract from the ox.

WALTER H. NADLER, M.D.

**Turpin, R., Chassagne, P., and Lefebvre, J.: Prepuberal Megalothymus; Planigraphic Studies of the Thymus in the Course of Development** (La megalothymie prepubertaire etude planigraphique du thymus au cours de la croissance). *Ann. d'endocrinol.*, 1939–1940, 1: 358.

For a long time anatomists have thought that the thymus reaches its maximum weight at the end of the twelfth year. After this there is rapid regression. However, more recent researches coming from different sources and based on the results of the comparison of a number of weights have shown that this was inexact. In fact, the weight of the thymus, instead of diminishing at the end of the twelfth year, increases during the course of development and reaches its maximum at the moment of puberty. After that it diminishes in size rapidly. Nevertheless, in spite of this increase in size the thymic development remains always proportionately less than that of the organism in general.

The error of the classical anatomists and the long incertitude relating to thymic evolution are easily understood if one bears in mind the extreme variability of this gland. It is well known that it is remarkably influenced by toxic infectious processes, and in addition, by avitaminoses and chronic suppuration. Its size decreases rapidly under their influence. After recovery has taken place, however, the thymus regains its normal weight and its entire aspect that existed before illness. These physiological and pathological variations of the thymus explain the errors of many of the previous investigations. If one is to be exact in the normal variations of the thymus in the course of development it is necessary to study only normal children whose weight and height correspond to the normal average for that age and whose state of nutrition is altogether satisfactory.

The difficulties of roentgenological interpretation of the thymic shadow are well known. Because of its position and its variation in size with crying or coughing, and during respiration, marked variations are observed. For this reason the authors have used the planigraphic method of study of the thymic shadow during the course of development. They used the planigraph of Ziedses des Plantes and describe their technique in detail. While approximately 200 children were studied by this method, the present report deals with 82, 35 of which were boys and 47 girls.

The authors conclude from these studies that in its normal state the thymus is accessible to planigraphic examination. If certain precautions which they indicate are observed, thymic measurements of the shadows obtained in both boys and girls from two to fifteen years of age can be measured and a graph made which parallels those variations found in the measurements of the normal organs made during the same period by the anatomists. The planigraphic method shows that the volume of the thymus increases during the course of development. This increase is discontinuous. It precedes the potential development of the organism. It reaches its maximum at the moment of puberty and its proportions are so sharply marked that one can speak of a prepuberal megalothymus. This prepuberal megalothymus goes along with the adiposity, the hyperthyroid function, and the other developmental potentialities of this age. In one of the observations it accompanied the precocious puberty seen in 1 girl who was six years and nine months of age. The maximum is a bit slower in boys than in girls.

The authors describe two main types of thymic shape in the prepuberal megalothymus, one like a heart and the other like a trapezoid. These aspects disappear one or two years after puberty. In the adolescent the thymic shadow is confused with the median vascular shadow.

The report is accompanied by several detailed charts, graphs, and typical roentgenographic illustrations of the various types of thymic shadows encountered.

NATHAN A. WOMACK, M.D.

**Albanese, A., and Scala, V.: A Report of the Relationship Between the Spleen, the Anterior Lobe of the Hypophysis, and the Ovary. Experimental Contribution** (Sui rapporti tra milza-preipofisi e ovaio. Contributo sperimentale). *Arch. di ostet. e ginec.*, 1939, 3: 501.

Aschheim and Zondek demonstrated functional interpendence between the anterior lobe of the hypophysis and the ovary. The ovarian function and the menstrual cycle depend upon the hormone of the anterior lobe; and the ovarian hormone, on the basis of recent experiments, is capable of inhibiting the function of the anterior lobe of the hypophysis.

Sakharoff tried to show the existence of a splenic leucolysin which regulated the white blood count counterbalanced by anti-leucolysin of hepatic origin. One of the authors (Scala) showed that there is a splenic leucolysin in which the spleen intervenes with a double mechanism: regulation and distribution. Kostitch and Telebakowitch, Ratassovleyvitch, and Wlatrovitch have shown that destruction of the spleen in the white rat activates the formation of ovarian hormone with the early appearance of the estrus. Subjecting the animals to hypersplenization with injection of splenic extract resulted in a retardation in appearance of the estrus in 13 of 18 animals. In the testis following splenectomy an active spermatogenesis without involution of the testis was obtained.

However, some investigators are not in agreement with these results; thus, Ehrhardt found no modification in the spermatogenesis; Asher and Pozzan, no alteration; and Winter, Krumbaar, and Kocher, no action in the ovarian cycle. Histologically, some authors found splenic hypertrophy following castration (Dionizi-Aschner-Marassini) in the dog and rat; some, no modification (Soli-Luciana); and some noted a diminution of volume (Moore-Braus-Bischoff). In the asplenic rabbit, following the injection of extract (testicular) there followed a pseudeosinophilic hyperleucocytosis (Businco-Takata).

Clinically, the manifestation of deficiency or incompleteness of the primary and secondary sexual characteristics, namely infantilism, hypo-evolutionism, hypogenitalism, or menstrual disturbance in some conditions in which there is a syndrome like splenomegaly, justifies the creation of a splenogenital syndrome (Radoslavlyeiyvh).

In malaria, Banti's disease, hemolytic icterus, and splenomegalic persistent cirrhosis of young people, there is absence of development of sexual characteristics. Infantilism is not caused by the disease but by the splenomegaly, and this is shown by the disappearance of the syndrome following splenectomy.

From these findings the authors conclude that in the function of the splenic-pituitary system there is an alternate influence of the various organs: a healthy metabolism may be derived from the spleen, pituitary gland, and gonads without any prolan.

The authors studied the immediate and remote effects of the pituitary hormone on the ovary and on the other organs in healthy animals and those without spleens. They first studied the different actions of increasing doses of prolan on the ovaries of healthy animals. They studied, in the healthy animal, the effect on the ovary of the grafting of spleens of animals subjected to strong doses of prolan.

The authors used young rabbits, three or four months old, weighing between 800 and 1,200 gm. The series contained more males than females at first. The animals were divided into various groups, according to the various doses of prolan. At the end of treatment the animals were killed and examined microscopically. Prolan was administered intramuscularly, the authors obtaining the best results by this means, notwithstanding the fact that intravenous injection has been advised to obtain the positive reaction of Friedman.

From the results obtained in these experiments the authors drew the following conclusions:

1. Splenectomy in young animals has not shown any modification in the ovarian activity.

2. In the rabbit, notwithstanding the intramuscular administration, the Aschheim-Friedman reaction has been obtained, and the minimum dose to obtain a slight reaction is 30 units in splenectomized rabbits and 40 units in non-splenectomized rabbits.

3. Histological modification with large doses of prolan is identical in the two groups of rabbits and does not permit a splenic interference in the prolan.

4. A small or average dose of prolan produces different changes in the asplenic animals than in the healthy animals, consisting in the former of greater activity and more advanced cellular manifestation.

The authors tried to study experimentally the rôle of the spleen in the relationship of the pituitary gland and the ovary. They noted that the spleen undoubtedly exercises its influence on prolan concentration. The authors agree with the hypothesis that the spleen functions as a defense organ, and they admit, though cautiously, a splenopituitary endocrine function. MICHAEL DEBAKEY, M.D.

**Rabald, E., and Voss, H. E.: The Occurrence and Characteristics of Lactation Hormones** (Ueber Vorkommen und Eigenschaften des Lactations-hormons). *Ztschr. f. physiol. Chem.*, 1939, 261: 71.

The authors preface this report with a discussion of the different elimination materials formerly utilized for obtaining the desired prolactins. Of all the excretions examined to date for obtaining prolactin, except that from the anterior lobe of the pituitary body, the urine of the lying-in patient appears to be the most productive; however, this assumes a rich lactational supply of the mother.

The authors examined the excretions of the liver of matured cattle, pigs, and horses without regard to sex or age of the animals. The estimates were conducted in accordance with the dove-tests of Riddle. To corroborate the macroscopic judgment in questionable cases, a histological examination of the thyroid gland was made and, in addition, a hema-

toxylin Sudan III stain of the scrapings of the thyroid gland was always made.

The liver extracts, when obtained from healthy cattle and pigs, were positive in the dove test if the injected quantity was not below 5 mgm. The yield obtained from the liver of cattle was about 100 times greater than that produced by the pituitary body. The yield of livers of horses (old or sick?) was always negative. A method in accord with that of Riddle and Bates for the preparation of the hormones was given in detail. On the basis of the reported results of the chemical analyses, and the agreement of biologically proved results the authors believe that the lactation hormones from the anterior lobe of the pituitary body and those of the liver are probably identical. (HERRNBERGER). MATHIAS J. SEIFERT, M.D.

**Eidelsberg, J., and Ornstein, E. A.: Observations on the Continued Use of Male Sex Hormone Over Long Periods of Time.** *Endocrinology*, 1940, 26: 46.

Clinical results are briefly reported in the cases of 4 young men who had infantile genitalia and complete lack of libido and erections; 3 of these had undescended testicles. After treatment with testosterone propionate there were symptoms and signs of masculinity, and the general well being, strength, and mental state improved markedly. On several occasions, because of too numerous erections and too pronounced libido, the dose or frequency of injections had to be decreased. No ill effects were noted. The average maintenance dose seemed to be between 50 and 75 mgm. per week, with individual variations. The patients were taught to administer their own injections after attaining the maintenance dosage. In 2 cases the prostate increased in size. Variable enlargement, but with no abnormal increase in size of the penis, occurred in each instance. Thyroid administration was more effective during the use of testosterone. The authors mention that sterile, compressed, pure testosterone-propionate tablets implanted under the skin were still effective after a period of from eight to ten weeks.

WALTER H. NADLER, M.D.

**McCullagh, E. P., and McGurl, F. J.: The Effects of Testosterone Propionate on Epiphyseal Closure, Sodium and Chlorine Balance, and on Sperm Counts.** *Endocrinology*, 1940, 26: 377.

These writers state that until 1938 they had never seen epiphyseal development in eunuchoidism which advanced beyond the normal rate with testis hormone. However, recent observations on three eunuchs treated intensely with testosterone propionate revealed epiphyseal union which took place at a more rapid rate than normal. One patient who had received from 30 to 60 mgm. of testosterone propionate per week for a period of five months showed no advance in bone age, whereas when the dose was increased to 75 mgm. and maintained for eight months, the bone age was advanced three years.

Two eunuchs were observed for weight gain, and sodium, chloride, and nitrogen excretion during a three-day control period and for six days following the administration of 50 mgm. of testosterone propionate. A gain of 4¾ and of 5 lb. respectively was observed. It must be noted, however, that the patients were receiving 2,388 calories daily. There was a marked diminution in the urinary sodium and urinary chloride following treatment, the diminution of the sodium being more marked than that of the chloride. No change was observed in the nitrogen excretion.

In each of these treated cases there was a decided diminution in the total number of sperm produced during treatment.

These writers wisely warn against the injudicious use of larger doses of testosterone. They point out that large doses in immature individuals may produce early epiphyseal union and subsequent dwarfing. They suggest that the same result might be obtained with the use of any substance capable of stimulating the testis to produce larger than normal quantities of androgens. They also point out that caution should be exercised when fertility is to be preserved because of the fall in sperm production observed in patients who have been treated with this drug. RULON W. RAWSON, M.D.

## EXPERIMENTAL SURGERY

**Murray, G. D. W.: Heparin in Thrombosis and Embolism.** *Brit. J. Surg.*, 1940, 27: 567.

With the marked improvement in the manufacture and purification of heparin it was decided to determine the effect of its use on experimental and clinical cases of thrombosis and embolism. In cases of artificially produced injury to veins, there was a very marked decrease in the number of veins which showed thrombosis. Moreover, in cases of arterial and venous grafts, there was a very large percentage of satisfactory results without signs of intravascular clotting. When heparin was not used many cases of thrombosis were reported. One venous graft in the popliteal space in a human being was made possible through the use of heparin.

In more than 400 cases, heparin has been employed and the results cited would tend to substantiate the claim of its value in clinical practice. It has been successfully employed to prevent thrombosis in vessels receiving continuous intravenous medication; in the follow-up care of arterial embolectomies; in thrombophlebitis, and in pulmonary embolism. Twelve cases of arterial embolectomy are reported which were carried out successfully with its use. The arteries of 2 patients who died were carefully examined and the intima was found to be quite free of clot. This is in contrast to the usual experience, in which the greatest danger of the operation lies in the reformation of thrombotic material. In the case of thrombophlebitis, however, some of the most striking clinical results have been noted: the pain, temperature, and swelling have

been markedly decreased in a short time. In none of the 50 cases so treated was there any pulmonary embolism. In 600 cases of thrombophlebitis not treated with heparin the incidence of pulmonary embolism was 15 per cent.

The reasons for these improved results are not easy to determine but they seem no less definite on that account. The average case was treated with heparin for about ten days. In some cases this was continued longer before the temperature returned to normal. After four days the patient is advised to move actively around in bed, and after two days more he is given active exercise in preparation for getting up. He is gotten up between the tenth and the twelfth day and if there is no recurrence of temperature, he is allowed to leave the hospital.

It is in pulmonary embolism that this material appears to give some of its most dramatic results. Twenty-two patients were treated with heparin, and none died of embolism though death seemed imminent for some. Symptomatically and clinically they showed marked improvement. Two patients who had pulmonary embolism and were treated with heparin died and autopsies were made. The death of one was clearly due to peritonitis. The other had recovered from his embolisms sufficiently to leave the hospital and return to work, but subsequently he had to be operated upon for an intestinal obstruction. Because of the fact that he also had a bleeding duodenal ulcer at this time, it was deemed inadvisable to administer heparin, and he promptly died of massive pulmonary embolism following the second operation.

In cases of mesenteric thrombosis and splenectomy, the material has been used to apparent advantage. Four patients recovered from the first condition while 2 who failed to survive showed no increase in the thrombosis at death. The deaths were attributed to peritonitis. Portal thrombosis which is a serious complication in splenectomy was not noted in 8 cases when heparin was used; 2 patients died but at autopsy no thrombosis was seen.

In postoperative cases, heparin is ordinarily not given for from four to twenty-four hours, in order not to encourage bleeding from the wound site. The injection is then continued until the patient has regained normal activity, i.e., when the factors thought to contribute to the production of thrombosis have ceased to act. This time has been reached when shock has passed and the blood pressure and circulation are normal; the incision has healed and is not painful so that deep respirations are possible; the patient feels well and energetic and moves about actively in bed, and can exercise; distention is gone; the appetite has returned and the gastrointestinal and urinary functions have returned to normal; the chest is clear; and the temperature and pulse have returned to normal. Before starting treatment, the blood clotting time, prothrombin index, platelet count, bleeding time, and other ordinary blood analyses must be ascertained.

JOHN WILTSIE EPTON, M.D.

**Lipschuetz, A., and Vargas, L., Jr.: Tumorigenic Powers of Stilbestrol and Follicular Hormones.** *Lancet*, 1940, 238: 541.

The authors had shown previously that stilbestrol was capable of forming small fibroid tumors in the uteri of guinea pigs when the substance was administered over a prolonged period of time. In the present work the tumorigenic action of stilbestrol was compared with the similar action of natural hormones, i.e., estradiol and estrone. Stilbestrol was found to possess a greater action in the production of these small fibroid tumors than the natural hormones, but this action was about the same as that obtained with certain esters of estradiol.

The authors are of the opinion that stilbestrol is inactivated by the organism at a much slower rate than are the natural hormones, and is consequently more toxic.

LUTHER H. WOLFF, M.D.

**Brues, A. M., Marble, B. B., and Jackson, E. B.: Effects of Colchicine and Radiation on the Growth of Normal Tissues and Tumors.** *Am. J. Cancer*, 1940, 38: 159.

The use of colchicine produces pronounced effects, such as arrest of mitosis and various other cytological abnormalities. The fact that it disturbs the process of mitosis has led some investigators to believe that it might be valuable in the therapy of tumors. Considerable doubt exists, however, as to the influence of this alkaloid on the total growth when it is administered chronically. The results of investigations thus far appear somewhat contradictory. While some investigators report encouraging results following the use of colchicine in the case of experimental tumors, others report that colchicine fails to affect tumor growth.

The consideration of this problem is further complicated by the fact that colchicine has a two-fold action, namely, a stimulating action as well as a destructive action, a mitotic as well as a toxic effect, which may be entirely dissociated. It is well known that colchicine in sublethal amounts produces hemorrhages in various organs. This is true especially in experimental sarcoma. Thus, the regression of the tumors may be the result of hemorrhagic processes and may bear little relation to the inhibition of mitosis. In the presence of both stimulation and destruction, either hypertrophy or atrophy of the tissues could occur.

In the present study the authors have sought to determine the effects of daily treatment with colchicine upon the growth of tumors and regenerating tissues in experimental animals, using for this purpose both mice and rats. There is a narrow range of dosage for colchicine which brings about the characteristic effect upon cell division and which may be administered daily without causing death. The authors used corresponding amounts in their experiments. The effects of radiation in combination with the use of colchicine were likewise studied. The probability that cells are most susceptible to the effects of roentgen radiation at some stage of mitosis

led the authors to investigate the effect of daily irradiation of tumors at a time when the numbers of mitoses arrested by colchicine were presumably at their height. While the study was in progress it became evident that no notable retardation of tumor growth was effected by the colchicine, and the authors concluded that the results might be due to failure of the drug to penetrate into the deeper parts of the tumor tissue, since it had been previously determined that the cytological effects sometimes manifested themselves only at the periphery of large tumors. In one group of experimental animals, therefore, the authors performed successive radical operations in an effort to affect recurrences and metastases growing from small nests of cells, into which presumably the drug might readily penetrate. An investigation of the content of reducing substances in chronically treated tumors was also made in order to corroborate or deny the assertion of other investigators that a notable reduction of ascorbic acid is found in tissues and tumors of animals receiving large doses of colchicine. The authors present a complete description of the number and kind of experiments undertaken, together with the technique employed in each instance and the type of response observed in each group of experiments.

Their results emphasize the fact that the treatment of tumor-bearing rats and mice with maximal sublethal daily dosage of colchicine throughout the life of the animals produces no evidence of retardation of tumor growth or of prevention of recurrences or metastases after tumor excision. These smaller doses produce profound alterations in the mechanism of mitosis, notably the arrest of many mitoses at the metaphase. While these doses may be given daily covering a long period of time, they do not cause any regression of the neoplasms. Moreover, they consistently failed to bring about any significant changes in the growth rates of the tumors studied. Likewise, it has appeared that there is no retardation of cell multiplication in the course of recovery from partial hepatectomy following the continued administration of colchicine. What is more, any retardation of cell multiplication does not manifest itself until the animals are near death and sections of liver tissue show evidence of tissue damage. Cell multiplication in the course of liver hypertrophy under similar conditions of dosage, frequently continues at a normal rate and appears to do so in the complete absence of normal karyokinesis.

With reference to large doses of colchicine, however, the authors were able to verify the observation previously made that colchicine retards tumor growth. The authors consider as large doses those which are dangerously close to the lethal amount, which cannot be repeated daily with impunity, and which cause hemorrhage and metabolic changes in tumors.

The experiments further established the fact that colchicine has no effect on the radiation response. The absence of synergism between colchicine and radiation indicates that cells resting in an abnormal metaphase are not particularly susceptible to destruction by the roentgen rays. Leaving aside any decision as to whether the regression of tumors is due to the direct effect of radiation on mitosis or to more complex circumstances, the authors point out that their data show that colchicine does not even decrease the latent period between irradiation and the various stages of regression, as might be expected if regression depended upon the destruction of cells which were in mitosis at the time radiation was given.

Analysis of tumor tissue for ascorbic acid showed no striking difference between the groups which were treated with colchicine and the control groups. The ascorbic-acid fraction appears to have been lowered in irradiated animals.

The authors state that the present study seems to establish, wholly aside from the question of initial stimulation, inhibition, or nuclear death, that cell increase over a prolonged period may occur at a normal rate with colchicine, as if this were regulated by normal metabolic influences or at least unhindered by the changes in nuclear division. It is suggested that the growth rate may be altered when the normal metabolic state is broken down, as reflected in the decreased Vitamin-C content of tissue after large doses. It is believed that the apparent arrest of mitosis in the tissues studied is in reality only a prolongation, and in some cases a modification of certain stages of cell division, which fails to hinder multiplication of cells over a prolonged period.

MATHIAS J. SEIFERT, M.D.